

Long COVID 1 year after hospitalisation for COVID-19: a prospective bicentric cohort study

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Summary

AIMS OF THE STUDY: There is increasing interest in better understanding of long COVID, a condition characterised by long-term sequelae — appearing or persisting after the typical convalescence period — of coronavirus disease 2019 (COVID-19). Herein, we describe long-term outcomes regarding residual symptoms and psychological distress in hospitalised patients 1 year after COVID-19.

METHODS: This prospective cohort study included consecutive adult patients hospitalised for confirmed COVID-19 in two Swiss tertiary-care hospitals between March and June 2020. The primary endpoint was evidence of long COVID 1 year after discharge, defined as ≥ 1 persisting or new symptom related to COVID-19, from a predefined list of symptoms. Secondary endpoints included psychological distress and symptoms of post-traumatic stress disorder (PTSD).

RESULTS: Among 90 patients included in the study, 63 (70%) had symptoms of long COVID 1 year after hospitalisation, particularly fatigue (46%), concentration difficulties (31%), shortness of breath (21%) and post-exertion malaise (20%). Three predictors, namely duration of hospitalisation (odds ratio [OR] 1.11, 95% confidence interval [CI] 1.00–1.22; $p = 0.041$), severity of illness (OR 1.19, 95% CI 1.04–1.37; $p = 0.013$), and self-perceived overall health status 30 days after hospitalisation (OR 0.97, 95% CI 0.94–1.00; $p = 0.027$) were associated with long COVID. Regarding secondary endpoints, 16 (18%) experienced psychological distress and 3 (3.3%) patients had symptoms of PTSD.

CONCLUSION: A high proportion of COVID-19 patients report symptoms of long COVID 1 year after hospitalisation, which negatively affects their quality of life. The most important risk factors were severe initial presentation of COVID-19 with long hospital stays.

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is responsible for the coronavirus disease 2019 (COVID-19) pandemic, which has resulted in a global healthcare crisis affecting millions of patients worldwide. Whereas the initial focus was on the acute in-hospital treatment of patients, there are increasing reports of persistent and prolonged effects after acute COVID-19 – a syndrome called long COVID [1–5].

Long COVID has been defined as residual symptoms after acute disease, which persist for more than 4 weeks [6]. A recent systematic review found that almost three in four patients still suffer from sequelae several months after recovery from acute illness [3]. Long COVID may afflict a wide range of organ systems, with the most commonly reported symptoms being shortness of breath, chronic fatigue, cognitive impairment, cough and chronic pain syndromes [3, 4]. The pathophysiological mechanisms underlying long COVID are still incompletely understood and diagnostic consensus criteria have not yet been defined. The current literature considers direct viral toxicity, immune dysregulation with prolonged inflammation, endothelial and microvascular damage, or adverse effects of received treatments as potential triggers or mediators of long COVID [6–9]. Especially older patients, and patients with high symptom load and severe course of the disease appear to be at higher risk for developing long COVID [10–12].

Symptoms such as fatigue, pain, or mental sequelae were already seen in connection with other coronavirus diseases such as severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), and were prevalent in follow-ups of up to 15 years [13–17]. Further, several studies showed that patients with acute COVID-19 frequently experience psychological distress. According to a recent meta-analysis, about 17% (95% CI 10% to 23%)

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of patients suffer from anxiety, 38% (95% CI 29% to 46%) from depression and 42% (95% CI 9% to 74%) from symptoms of post-traumatic stress disorder (PTSD) [18]. Recent studies suggest that a substantial number of patients continue to suffer from mental health problems with around one fourth of patients reporting symptoms of anxiety, depression, and post-traumatic stress, several weeks to months later [3, 5, 19–21]. Yet for COVID-19, most studies have only followed patients for 3 to 6 months. Hence data regarding the persistence of long COVID symptoms and longer-term risks are scarce.

Our aim was to assess the prevalence of persisting symptoms suggestive of long COVID, as well as psychological distress and PTSD in patients 1 year after hospitalisation for COVID-19, and to understand risk factors associated with long COVID.

Materials and methods

Study setting

This prospective bicentric cohort study was conducted at two tertiary care hospitals in Switzerland, the University Hospital Basel, and the Kantonsspital Aarau, from March 2020 to July 2021. The local Ethics Committee (Ethics Committee Northwest and Central Switzerland, EKNZ) approved the study. All participating patients provided written informed consent. This manuscript adheres to the STROBE statement [22].

Study population

Patients with COVID-19 who were consecutively admitted for inpatient care during March to June 2020 were eligible for inclusion. Patients were hospitalised based on their clinical condition, clinical risk factors (e.g., age >65 years, respiratory rate >25/min, hypoxaemia or pulmonary infiltrates observed on chest imaging). Patients were excluded from our study if they had insufficient proficiency in one of the local languages, cognitive impairment such as dementia or serious psychiatric conditions (e.g., psychosis). Clinical patient characteristics and severity or duration of COVID-19 were no reasons for exclusion. We contacted patients about 1 month after hospital discharge, informed them about the aim of our study and asked for consent to participate. We sent a letter containing the study information and informed consent form, and included those patients who provided written informed consent.

Data collection

Predictor variables and measures

Data were prospectively collected upon hospitalisation by specifically trained research staff. We reviewed patients' medical records from their hospitalisation with COVID-19 to collect sociodemographic factors (e.g., age, gender, citizenship), vital signs and illness-related characteristics. Specifically, we calculated the National Early Warning Score (NEWS) [23], a commonly used tool to assess a patient's severity of illness and detect patients prone to clinical deterioration. The NEWS is a scoring system that assesses the following physiological parameters: respiratory rate, oxygen saturation, temperature, systolic blood pres-

sure, heart rate and level of consciousness. To each parameter a score between 0 and 3 is allocated, depending on how much the parameter deviates from its normal range. A sum score of 7 reflects a high risk for clinical deterioration.

In addition, we assessed patients' severity of comorbidity using the Charlson Comorbidity Index (CCI) [24], intensive care unit (ICU) duration, intubation and duration of hospitalisation.

To assess the short-term health status of patients, specifically trained research staff conducted telephone interviews 30 and 90 days after hospital discharge. These structured interviews included internationally established, validated questionnaires as well as some items specifically designed for the purpose of this study (symptoms limiting life quality, predominant symptom, most concerning symptom). Psychological distress was assessed via the Hospital Anxiety and Depression Scale (HADS) as defined below [25]. We assessed patients' self-perceived overall health status using the visual analogue scale (VAS) of the EuroQol index ranging from 0 (worst imaginable health) to 100 (best imaginable health) [26, 27]. We evaluated patients' resilience through the 10-item version of the Connor-Davidson Resilience Scale (CD-RISC-10). The CD-RISC is commonly used in clinical research to assess resilience based on how well a person can cope with stress [28].

Finally, we determined patients' perceived stress through the Perceived Stress Scale (PSS-10) [29]. The PSS is a widely used instrument to measure the perception of stress and whether people appraise life events as unpredictable or uncontrollable.

Outcome variables and measures

In a follow-up telephone interview 1 year after hospital discharge, specifically trained research staff assessed primary and secondary outcomes as outlined below.

Primary endpoint: The primary endpoint of our study was long COVID 1 year after hospitalisation, defined as the presence of at least one persisting symptom which newly occurred during or after acute infection with SARS-CoV-2. This definition of long COVID was based on previous studies [3, 4] and included different symptoms known to be associated with COVID-19, including shortness of breath, fatigue, cough, chest pain/tightness, dysosmia, dysgeusia, sleep disorders, headache, concentration difficulties, joint pain, muscle pain, palpitations, post-exertion malaise, loss of appetite or nausea, vomiting or diarrhoea, fever, paraesthesia, skin disorders (rash, pruritus) and other symptoms related to patients' initial COVID-19. Patients also rated the intensity of symptoms on a VAS (ranging from 0 – not at all to 10 – very much).

Secondary endpoints: Secondary endpoints included psychological distress, defined as clinically relevant symptoms of anxiety and/or depression 1 year after discharge, measured with the HADS [25]. In line with previous research, a score of ≥ 8 on the depression and/or anxiety subscale (range: 0 to 21) of the HADS, indicating clinically relevant symptoms of depression and/or anxiety, was defined as clinically relevant psychological distress [25, 30]. Further, we assessed symptoms of PTSD through a German translation of the Impact of Event Scale-revised (IES-r), which measures symptoms of emotional distress caused

by traumatic events [31]. The IES-r is a 22-item questionnaire containing three subscales covering the three symptom domains intrusion, avoidance and hyperarousal. A cut-off score of 1.5 was considered to indicate clinically relevant symptoms of PTSD as suggested in previous research [32].

During the interview, interviewers filled out a printed questionnaire form, entered the data into an electronic data file and conducted quality control for each variable.

Statistical analyses

Descriptive statistics, i.e., frequencies as well as means and standard deviations were used to present characteristics of the study population. To investigate the associations of potential risk and protective factors assessed at 30-day follow-up and outcomes at 1-year follow-up, we used logistic regression models. Multivariable regression models included age, gender and the factors significantly associated with the outcome in univariable analyses. We report odds ratios (ORs) and 95% confidence intervals (CIs) as a measure of association and the area under the receiver operating characteristic curve (AUC) as a measure of discrimination. A p-value of <0.05 (two-tailed) was considered statistically significant. All statistical analyses were conducted using Stata 15 (Stata Corp, College Station, Texas, USA).

Results

Study sample

Between March and June 2020, 301 patients with COVID-19 were hospitalised at the University Hospital of Basel (n = 198) and Kantonsspital Aarau (n = 103). Figure 1 shows the flowchart of patients regarding study inclusion. Forty-one patients had died before the end of follow-up, 86 met exclusion criteria such as insufficient proficiency in the local language, cognitive impairment or severe underlying psychiatric conditions, 59 were not reachable by phone and 25 did not provide informed consent or did not want to participate any further. The final sample therefore consisted of 90 patients.

The mean age of patients at hospitalisation was 60 years and 38% were female. The mean duration of hospitalisation was 9.4 days. Overall, there was a high burden of comorbidities with a CCI of 2.4, and 17% of patients required treatment in the intensive care unit (ICU). Patients who required ICU treatment were 58 years old and 27% were female. These patients stayed for 9 days in the ICU and for 18 days in the hospital. Additional sociodemographic and clinical characteristics of patients, as well as outcomes after 1 year are shown in table 1.

Primary endpoint: long COVID 1 year after hospitalisation

One year after hospitalisation, 63 (70%) patients had symptoms of long COVID and thus met our definition of the primary endpoint (table 1). The most common symptoms experienced were fatigue (46%), concentration difficulties (31%), shortness of breath (21%) and post-exertion malaise (20%). Thirty-four (38%) patients indicated that their symptoms limited their quality of life. A total of 34% of patients reported one or two symptoms, and 36% reported ≥ 3 symptoms after 1 year. Figures 2 and 3 show the distribution of symptoms overall and the most important symptoms at 90 days and 1 year among patients in our cohort. The frequency of symptoms was relatively similar at 90 days and 1 year.

Associations of predictor variables with long COVID

We investigated associations between several predictor variables and long COVID (table 2). Three acute illness-related factors were associated with long COVID in univariable analyses, including duration of hospitalisation (OR 1.11, 95% CI 1.00–1.22; p = 0.041), severity of illness according to NEWS (OR 1.19, 95% CI 1.04–1.37; p = 0.013) and self-perceived overall health status (EuroQol) 30 days after hospitalisation (OR 0.97, 95% CI 0.94–1.00; p = 0.027). There were no significant associations of sociodemographic and psychological factors assessed at 30-day follow-up and the prevalence of long COVID at 1 year.

To further investigate the prognostic value of these predictors regarding long COVID, we calculated a multivariable model including age, gender and the three significant predictors. Results showed moderate discrimination of this model with an area under the receiver-operating character-

Figure 1: Flow diagram of the study population.

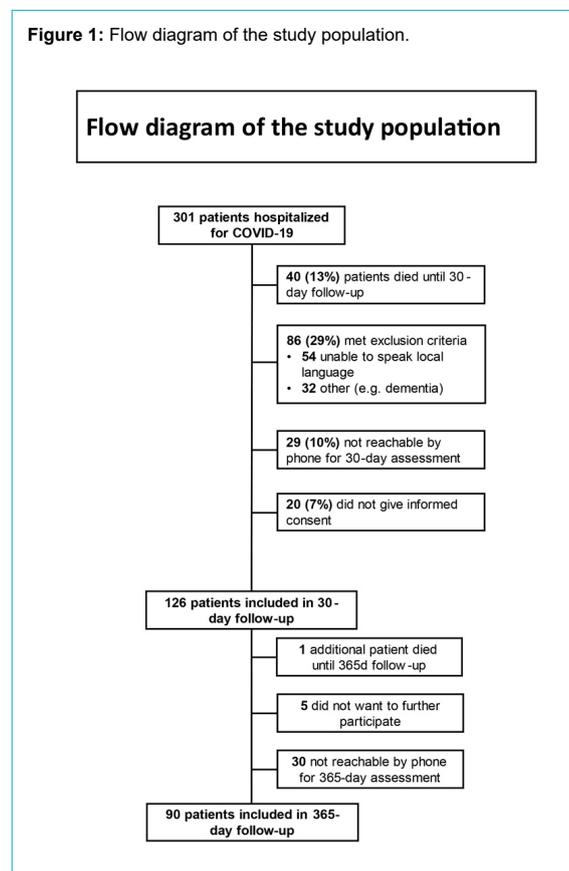


Table 1:
Characteristics of the study population.

Factor	Value (n = 90)	
<i>Sociodemographic factors</i>		
Age (years), mean (SD)	60.09 (15.14)	
Gender (female), n (%)	34 (38%)	
Citizenship, n (%)	Swiss	66 (74%)
	Non-Swiss	23 (26%)
Religious affiliation, n (%)	Christian	50 (57%)
	Non-Christian	8 (9%)
	Not religious	30 (34%)
Civil status, n (%)	Married/partnership	60 (67%)
	Widowed/separated/single	29 (33%)
Having children (yes), n (%)	61 (72%)	
Education, n (%)	High School	6 (7%)
	Apprenticeship	58 (68%)
	College/university	21 (25%)
<i>Acute illness-related factors</i>		
Duration of hospitalisation (days), mean (SD)	9.44 (6.77)	
Severity of illness (NEWS score), mean (SD)	6.60 (3.61)	
Comorbidity (CCI), mean (SD)	2.36 (2.12)	
ICU stay, n (%)	15 (17%)	
Requirement of oxygen, n (%)	None	30 (34%)
	Nasal canula/NIV	49 (55%)
	Intubation	10 (11%)
<i>Psychological factors at 30-day follow-up</i>		
	mean (SD)	
Anxiety symptoms (HADS-A)	4.01 (3.74)	
Depressive symptoms (HADS-D)	2.53 (3.26)	
PTSD symptoms (IES-r)	-2.5 (3.26)	
Perceived stress (PSS-10)	21.9 (7.54)	
Self-perceived overall health status (EuroQol VAS 0-100)	73.82 (17.08)	
Resilience (CD-RISC)	31.65 (6.04)	
<i>Long COVID symptoms one year after hospitalisation</i>		
	n (%) / mean (SD)	
overall	63 (70%)	
Shortness of breath	19 (21%)	
– if yes, intensity (VAS 0-10)	4.16 (1.68)	
Fatigue	41 (46%)	
– if yes, intensity (VAS 0-10)	5.54 (2.34)	
Cough	6 (7%)	
– if yes, intensity (VAS 0-10)	4.17 (1.17)	
Chest pain/tightness	11 (12%)	
– if yes, intensity (VAS 0-10)	4.18 (2.52)	
Dysosmia	14 (16%)	
– if yes, intensity (VAS 0-10)	4.43 (2.47)	
Dysgeusia	11 (12%)	
– if yes, intensity (VAS 0-10)	4.27 (2.24)	
Sleep disorder	15 (17%)	
– if yes, intensity (VAS 0-10)	5.67 (2.41)	
Headache	8 (9%)	
– if yes, intensity (VAS 0-10)	3.25 (2.19)	
Concentration difficulties	28 (31%)	
– if yes, intensity (VAS 0-10)	5.11 (1.99)	
Joint pain	16 (18%)	
– if yes, intensity (VAS 0-10)	5.06 (2.29)	
Muscle pain	13 (14%)	
– if yes, intensity (VAS 0-10)	5.08 (2.60)	
Palpitations	9 (10%)	
– if yes, intensity (VAS 0-10)	4.33 (2.40)	
Post-exertion malaise	18 (20%)	
– if yes, intensity (VAS 0-10)	5.28 (2.30)	
Loss of appetite / Nausea	6 (7%)	
– if yes, intensity (VAS 0-10)	4.83 (1.72)	
Vomiting/Diarrhoea	5 (6%)	
– if yes, intensity (VAS 0-10)	7.00 (2.45)	

Fever		2 (2%)
Paraesthesia		7 (8%)
– if yes, intensity (VAS 0-10)		5.00 (3.11)
Skin disorders (Rash, pruritus)		5 (6%)
– if yes, intensity (VAS 0-10)		4.80 (2.28)
Other		10 (11%)
– if yes, intensity (VAS 0-10)		4.70 (2.71)
Symptoms limiting quality of life (yes), n (%)		34 (38%)
Which is the predominant symptom?	Fatigue	18 (28%)
	Dyspnoea	9 (14.29%)
	Concentration difficulties	9 (14.29%)
	Joint pain	6 (9.5%)
	Post-exertion malaise	3 (4.76%)
Which is the most concerning symptom?	Fatigue	8 (12.7%)
	Concentration difficulties	8 (12.7%)
	Dyspnoea	6 (9.5%)
	Post-exertion malaise	5 (7.94%)
	Joint pain	4 (6.35%)
<i>Psychological outcomes one year after hospitalisation</i>		
Self-perceived overall health status (EuroQol VAS 0-100), mean (SD)		77.11 (16.01)
Anxiety symptoms (HADS-A), n (%)		11 (13%)
Depressive symptoms (HADS-D), n (%)		9 (10%)
Anxiety and/or depressive symptoms (HADS), n (%)		16 (18%)
PTSD symptoms (IES-r), n (%)		3 (3.33%)

SD: standard deviation; HADS-A: anxiety subscale of the Hospital and Anxiety Depression Scale; HADS-D: depression subscale of the Hospital and Anxiety Depression Scale; PTSD: post-traumatic stress disorder; IES-r: Impact of Event Scale revised; PSS-10: Perceived Stress Scale; CD-RISC: Connor-Davidson Resilience Scale; VAS: visual analogue scale; NEWS: National Early Warning Score; CCI: Charlson Comorbidity Index; ICU: intensive care unit

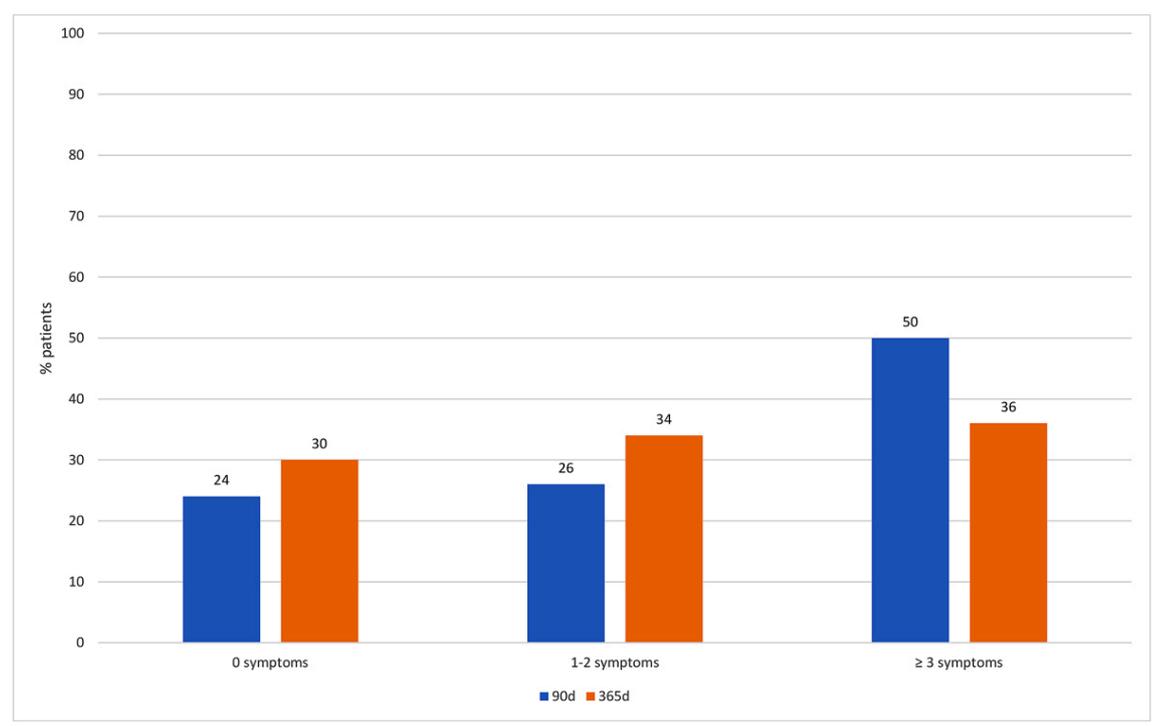
istic curve (AUC) of 0.75 (supplementary table S1 in the appendix).

Secondary endpoints: psychological outcomes 1 year after hospitalisation

Sixteen patients (18%) experienced psychological distress, i.e., symptoms of depression and/or anxiety (table 3). Nine patients reported only anxiety, two only depression and

five patients had both. Psychological factors at 30-day follow up were associated with psychological distress 1 year after hospitalisation: Anxiety symptoms (OR 1.25, 95% CI 1.07–1.45; $p = 0.004$), depressive symptoms (OR 1.45, 95% CI 1.15–1.82; $p = 0.002$), perceived stress (OR 1.11, 95% CI 1.02–1.22; $p = 0.015$) and resilience (OR 0.83, 95% CI 0.74–0.93; $p = 0.002$). There was no association between sociodemographic and acute illness-related factors and outcomes. Three patients (3.3%) had clinical-

Figure 2: Number of persistent symptoms 90 and 365 days after hospitalisation.



ly relevant symptoms of PTSD at 1 year follow-up. There were no differences in the rates of psychological distress in patients with and without long COVID. Of the 61 patients with long COVID, 10 (16.4%) showed psychological distress and 51 (83.6%) did not ($p = 0.513$). Of 39 patients with fatigue, 9 (23.1%) experienced psychological distress whereas 30 (76.9%) did not ($p = 0.288$).

Discussion

The main finding of this two-centre, prospective cohort study is that 70% of patients report residual symptoms suggestive of long COVID 1 year after hospitalisation due to COVID-19. In more than a third of patients, symptoms were severe with a significant impact on quality of life, and 36% of patients reported ≥ 3 symptoms 1 year after infection. Additionally, 18% of patients suffered from psychological distress 1 year after hospitalisation for COVID-19. Several key findings need to be discussed.

Figure 3: Prevalence of the most common persistent symptoms 90 and 365 days after hospitalisation.

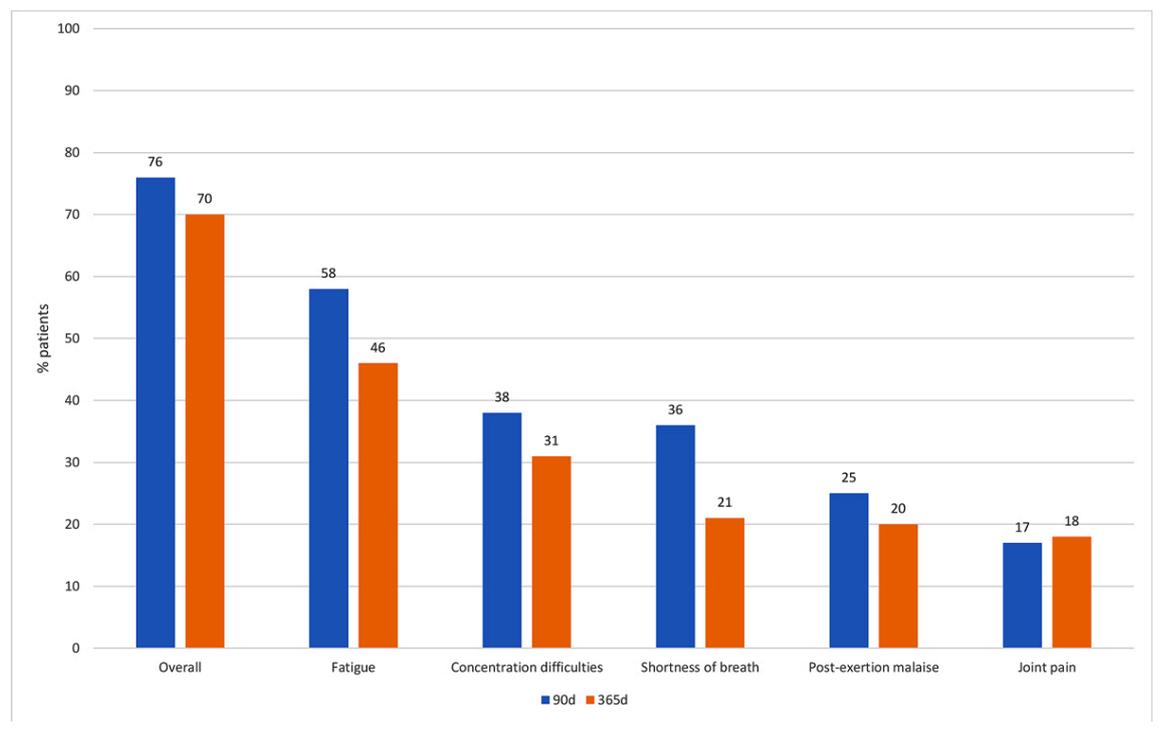


Table 2: Prevalence and factors associated with long COVID.

Factor	n	Long COVID (no) n = 27	Long COVID (yes) n = 63	Odds ratio, 95% CI	p-value
Age (years), mean (SD)	90	61.70 (17.13)	59.41 (14.30)	0.99 (0.96–1.02)	0.508
Gender (female), n (%)	90	13 (48%)	21 (33%)	0.54 (0.21–1.35)	0.187
Citizenship, n (%)	Swiss	21 (78%)	45 (73%)	1 (Ref)	
	Non-Swiss	6 (22%)	17 (27%)	1.32 (0.46–3.84)	0.607
Education, n (%)	High school/apprenticeship	18 (67%)	46 (79%)	1 (Ref)	
	College/university	9 (33%)	12 (21%)	0.52 (0.19–1.45)	0.212
Duration of hospitalisation (days), mean (SD)	90	7.11 (5.02)	10.45 (7.20)	1.11 (1.00–1.22)	0.041
Severity of illness (NEWS score), mean (SD)	90	5.11 (3.75)	7.24 (3.38)	1.19 (1.04–1.37)	0.013
Comorbidity (CCI), mean (SD)	90	2.59 (2.10)	2.26 (2.13)	0.93 (0.75–1.15)	0.492
ICU stay, n (%)	90	2 (7%)	13 (21%)	3.32 (0.69–15.86)	0.133
Anxiety symptoms 30 days after hospitalisation (HADS-A), mean (SD)	89	3.19 (2.54)	4.37 (4.12)	1.1 (0.96–1.27)	0.174
Depressive symptoms 30 days after hospitalisation (HADS-D), mean (SD)	89	1.93 (2.11)	2.79 (3.63)	1.1 (0.93–1.31)	0.258
PTSD symptoms 30 days after hospitalisation (IES-r), mean (SD)	87	–2.85 (1.49)	–2.34 (1.68)	1.24 (0.90–1.7)	0.183
Perceived stress during illness (PSS-10), mean (SD)	67	21.86 (6.51)	21.91 (8.04)	1 (0.93–1.07)	0.977
Self-perceived overall health status 30 days after hospitalisation (EuroQol VAS 0–100), mean (SD)	88	80.00 (15.38)	71.08 (17.20)	0.97 (0.94–1.00)	0.027
Resilience (CD-RISC) 30 days after hospitalisation, mean (SD)	79	32.31 (5.16)	31.32 (6.45)	0.97 (0.89–1.06)	0.494

SD: standard deviation; OR: odds ratio; CI: confidence interval; HADS-A: anxiety subscale of the Hospital and Anxiety Depression Scale; HADS-D: depression subscale of the Hospital and Anxiety Depression Scale; IES-r: Impact of Event Scale revised; PSS-10: Perceived Stress Scale; CD-RISC: Connor-Davidson Resilience Scale; NEWS: National Early Warning Score; CCI: Charlson Comorbidity Index; ICU: intensive care unit

First, our study shows that even 1 year after acute illness with COVID-19 a vast majority of patients still meet the criteria for long COVID and show at least one persistent symptom. The most common symptoms reported in our cohort (in order of decreasing frequency) were fatigue, concentration difficulties, shortness of breath, post-exertion malaise and joint pain. These results are largely in line with studies investigating the prevalence of long COVID in patients 3 to 6 months after COVID-19 [3–5, 33]. A recent meta-analysis reported residual symptoms in 72.5% of all patients between 2 and 7 months after acute infection [3]. Recent longer-term studies in outpatients indicated that between 39% and 53% of patients reported persisting symptoms after 7 to 12 months [34, 35]. The high proportion of patients with ongoing symptoms in our study may be explained by the fact that we only included hospitalised patients who presumably had a higher burden of disease and comorbidities. Correspondingly, we found illness-related factors to be associated with long COVID. In particular, patients with a longer duration of hospitalisation, more severe illness according to the NEWS during acute infection and lower self-perceived overall health status at baseline were at increased risk for developing long COVID. This finding is in line with previous studies with short-term follow-up, which demonstrated that high initial symptom load and disease severity are predictive for patients showing residual symptoms that go beyond the acute illness with COVID-19 [11, 36, 37].

Second, one in three patients reported at least three residual symptoms after COVID-19 and more than half of our patients with long COVID indicated a relevant impact of symptoms on daily life. Similarly, in a mixed cohort of outpatients and hospitalised patients, about one third of patients reported a persistent decline in health-related quality of life 9 months after COVID diagnosis [1]. Moreover, even a mild course of COVID-19 had a negative impact on psychosocial functioning [38, 39]. The long-term outcome in patients assessed beyond 9 months after acute ill-

ness with COVID-19 has not been well-described, so far. Our study adds to emerging evidence indicating that long COVID may well persist for more than 1 year after acute infection.

Third, we found that 18% of patients suffer from symptoms of anxiety and/or depression even 1 year after hospitalisation. The rates in our sample are higher than those in the general population in Switzerland in 2017 [40] and the European Union during 2013 to 2015 [41].

Although emotional distress during and shortly after the acute phase of COVID-19 may be self-limiting and thus does not necessarily require clinical care, several studies indicate that a substantial group of patients continues to suffer from clinically relevant symptoms of anxiety and depression up to 1 year later. A recent systematic review showed that about 15% of patients who had been diagnosed with COVID-19 suffered from persistent symptoms of depression and 22% from anxiety, which are both higher than in our sample [3]. However, the rates reported by the meta-analysis are based on 16 studies which mostly had follow-up durations of around 3 months and none followed patients for longer than 6 months. One of the included studies assessing Swiss patients 6 to 8 months after their COVID-19 diagnosis showed that 32% reported anxiety and 26% depressive symptoms [20]. As we assessed patients 1 year after hospitalisation, the longer follow-up duration might explain the lower rates in our sample compared with most other studies. Further, the higher rates of depression and anxiety in our sample at 1- and 3-month follow-up [42, 43], which more closely align with those of Nasserie et al. [3], suggest that the psychological symptoms might decrease over time. Additionally, differences in operationalisation of psychological distress might contribute to differences in the reported rates. Most studies analysed self-rated symptoms assessed with single items or questionnaires, and some evaluated psychiatric diagnoses. The latter emphasises the clinical relevance of the persisting psychological symptoms. Despite the high risk of

Table 3:
Prevalence and factors associated with psychological distress.

Factor	n	Psychological distress (no)	Psychological distress (yes)	Odds ratio, 95% CI	p-value
		n = 72	n = 16		
<i>Sociodemographic factors</i>					
Age (years), mean (SD)	88	60.88 (13.76)	57.06 (20.87)	0.98 (0.95–1.02)	0.365
Gender (female), n (%)	88	26 (36%)	6 (38%)	1.06 (0.35–3.26)	0.917
Citizenship, n (%)	Swiss	88	52 (73%)	12 (75%)	1 (Ref)
	Non-Swiss		19 (27%)	4 (25%)	0.91 (0.26–3.18)
Education, n (%)	High school/apprenticeship	83	54 (79%)	9 (60%)	1 (Ref)
	College/university		14 (21%)	6 (40%)	2.57 (0.78–8.44)
<i>Acute illness-related factors</i>					
Duration of hospitalisation (days), mean (SD)	88	9.42 (7.06)	9.63 (5.92)	1 (0.93–1.09)	0.914
Severity of illness (NEWS score), mean (SD)	88	6.54 (3.58)	6.63 (3.98)	1.01 (0.87–1.16)	0.928
Comorbidity (CCI), mean (SD)	88	2.41 (2.09)	2.19 (2.40)	0.95 (0.73–1.24)	0.708
ICU stay, n (%)	88	12 (17%)	2 (13%)	0.7 (0.14–3.5)	0.666
<i>Psychological factors at 30-day follow-up</i>					
Anxiety symptoms (HADS-A), mean (SD)	87	3.27 (3.16)	6.50 (4.46)	1.25 (1.07–1.45)	0.004
Depressive symptoms (HADS-D), mean (SD)	87	1.73 (1.95)	5.44 (5.15)	1.45 (1.15–1.82)	0.002
Perceived stress (PSS-10), mean (SD)	66	20.61 (6.28)	27.00 (10.42)	1.11 (1.02–1.22)	0.015
Resilience (CD-RISC), mean (SD)	77	32.98 (4.43)	26.40 (8.58)	0.83 (0.74–0.93)	0.002

SD: standard deviation; CI: confidence interval; HADS-A: anxiety subscale of the Hospital and Anxiety Depression Scale; HADS-D: depression subscale of the Hospital and Anxiety Depression Scale; PSS-10: Perceived Stress Scale; CD-RISC: Connor-Davidson Resilience Scale; NEWS: National Early Warning Score; CCI: Charlson Comorbidity Index; ICU: intensive care unit

symptoms of long COVID in our population, two thirds of patients did not have limitations to their quality of life, and we found no difference in psychological symptoms between long COVID and not long COVID patients after 1 year. Although our study was limited by low power, resilience, social support and other protective factors might have prevented further adverse health outcomes in patients. Early preventive strategies regarding long-term mental health problems in patients with COVID-19 should be assessed by future studies.

So far, evidence on potential predictors of long-term psychological distress is scarce. One Swiss study evaluating a cohort of mainly non-hospitalised patients found a lower level of education as well as unemployment to be associated with symptoms of depression 6 to 8 months after COVID-19 [20]. In our cohort of hospitalised patients, sociodemographic factors as well as severity of illness were not associated with long-term psychological distress. However, patients with higher levels of perceived stress, anxiety and depression at 1-month follow-up were more likely to experience psychological distress after 1 year. However, our sample was small and there is thus a risk for type II error.

Finally, fatigue, sleep disorders and concentration difficulties are potential symptoms of depressive and anxiety disorders, but also commonly described as long COVID symptoms. We assessed depression and anxiety with the HADS, which was developed for patients with somatic diseases and does not include these symptoms. In our study, patients with long COVID did not have higher rates of anxiety or depression than patients without residual long COVID symptoms. However, it must be noted that in our sample only a relatively small number of patients had anxiety or depression, potentially concealing a possible difference between the two groups. Nonetheless, considering the increased long-term prevalence of anxiety and depressive disorders in patients with COVID-19, affective disorders should be considered as potential differential diagnoses, especially in patients who solely present with fatigue, sleep disorders or concentration difficulties.

This study has limitations including the small sample size and selection bias due to our exclusion criteria. Particularly, the exclusion of almost 20% of patients owing to a lack of language skills might be a selection bias. As previous research has shown that being in an ethnic minority is often associated with psychological symptoms [44, 45], the prevalence of psychological distress in our study might be underrepresented. Also, we excluded a large proportion of patients due to dementia who were significantly older than the remaining patients of our cohort. As age is an important predictor of long COVID [3, 36], again the prevalence could be underestimated from our study.

We evaluated several symptoms suggested as symptoms of long COVID by previous studies. The specificity of these different symptoms to long COVID needs validation in future studies. The observational design does not allow any conclusions regarding preventive effects and the study is thus rather hypothesis-generating.

Further, we did not assess fatigue and neurocognitive deficits objectively but through inquiring via interview only. Fatigue might play an important role in patients with long COVID similar to that in patients with multiple sele-

rosis, as fatigue prevents patients from functioning normally and affects quality of life. We assessed quality of life through the EuroQol. Further research should incorporate other questionnaires such as the INTERMED self-assessment questionnaire to better evaluate the influence of long COVID on activities of daily life or social activities.

Finally, we only quantitatively assessed symptoms of long COVID. Future research should also focus on qualitative data to better understand this new disease entity.

Conclusions

A high proportion of COVID-19 patients report symptoms of long COVID 1 year after hospitalisation, which negatively affect their quality of life. The main risk factors are associated with severity of illness and may not be modifiable. There is need for further research into prevention and treatment of long COVID, particularly in patients with a high initial severity of illness.

Data sharing statement

We will share deidentified data of patients included in this study after finalisation of secondary projects and upon reasonable request. Proposals should be directed to sabina.hunziker[at]usb.ch.

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Conflicts of interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest was disclosed.

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Appendix: Supplementary table

Table S1:

Multivariable analyses of factors associated with long COVID.

Factor	n	Long COVID (no)	Long COVID (yes)	Multivariable OR, 95% CI	p-value	AUC
		n = 27	n = 63			0.75
Age (years), mean (SD)	90	61.70 (17.13)	59.41 (14.30)	0.98 (0.95–1.02)	0.298	
Gender (female), n (%)	90	13 (48%)	21 (33%)	0.51 (0.18–1.41)	0.192	
Duration of hospitalisation (days), mean (SD)	90	7.11 (5.02)	10.45 (7.20)	1.04 (0.93–0)	0.461	
Severity of illness (NEWS score), mean (SD)	90	5.11 (3.75)	7.24 (3.38)	1.15 (0.97–1.35)	0.104	
Self-perceived overall health status 30 days after hospitalisation (EuroQol VAS 0-100), mean (SD)	88	80.00 (15.38)	71.08 (17.20)	0.97 (0.94–1)	0.055	

SD: standard deviation; OR: odds ratio; CI: confidence interval; AUC: area under the curve; NEWS: National Early Warning Score