Long COVID in the Belgian Defence forces: prevalence, risk factors and impact on quality of daily functioning

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ABSTRACT

Introduction Long COVID (LC) is a medical condition first described and documented through anecdotes on social media by patients prior to being recognised by WHO as a disease. Although >50 prolonged symptoms of LC have been described, it remains a diagnostic challenge for military providers and therefore threatens operational readiness.

Methods On 9 September 2021, an online survey was emailed to 2192 Belgian Defence personnel who had previously tested PCR positive for SARS-CoV-2 between 17 August 2020 and 31 May 2021. A total of 718 validated responses were received.

Descriptive analyses determined the prevalence of LC and 10 most common symptoms and their duration following infection. In the explanatory analyses, risk factors related to LC were identified. To establish the health-related impact of LC on quality of life (HRQoL), we used the results from the EuroQol 5 Dimension 5 Level questionnaire.

Results The most frequent symptoms that were reported for >3 months were fatigue, lack of energy and breathing difficulties.

47.35% of the respondents reported at least one persistent symptom, while 21.87% reported more than 3 symptoms lasting for at least 3 months after the initial COVID-19 infection. Most patients with LC suffered from symptoms of a neuropsychiatric nature (71.76%).

LC was significantly associated with obesity; pre-existing respiratory disease and blood or immune disorders. Physical activity of >3 hours per week halved the risk of LC.

The total QoL is reduced in patients with LC. Considering the five dimensions of the questionnaire, only the self-care dimension was not influenced by the presence of LC.

Conclusions Almost half of Belgian Defence personnel developed LC after a confirmed COVID-19 infection, similar to numbers found in the Belgian population. Patients with LC would likely benefit from a multidisciplinary rehabilitation approach that addresses shortness of breath, fatigue and mood disturbance.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Long COVID (LC) remains a diagnostic challenge; even today clear and universally accepted definitions are lacking.
⇒ In a military population, prolonged symptoms might impact the operational readiness of soldiers; evaluating the prevalence, impact and related factors is therefore important, especially among young adults who could be affected for a greater proportion of their lives.

WHAT THIS STUDY ADDS

⇒ We found an overall prevalence proportion of almost half reporting at least one symptom of LC with fatigue or exhaustion, lack of energy, breathing difficulties and loss of smell as the most frequent symptoms lasting at least 3 months.
⇒ LC was found to be significantly associated with obesity, pre-existing respiratory disease and blood or immune disease.
⇒ Physical activity >3 hours/week reduced the risk of LC.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ LC has an important impact on the quality of life.
⇒ Multidisciplinary rehabilitation may be an important first step to protect employees.

INTRODUCTION

The disease long COVID (LC) was first described and documented on social media by patients prior to being officially recognised by WHO.[1] In October 2021, WHO defined the post-COVID-19 condition. According to the definition, LC occurs in individuals with a history of probable or confirmed SARS-CoV-2 infection, usually 3 months from the onset of the infection, with symptoms that last for at least 2 months and cannot be explained by an alternative diagnosis.[2]

More than 50 prolonged symptoms of LC have been described[3] including chest pain, difficulties with breathing, pain when breathing, painful muscles, ageusia or anosmia, tingling extremities, lump in throat, feeling hot and cold alternately, heavy arms or legs and general tiredness.[4]

LC remains a diagnostic challenge for many reasons including a high proportion of asymptomatic SARS-CoV-2 cases[5] and the lack of testing early in the pandemic.[6] Positive postinfectious serology may be useful, however, some patients may remain or become seronegative after infection.[7] SARS-CoV-2 has a multisystemic effect because the ACE receptor to which it binds is found in several tissues. Broad analysis of relevant scientific publications suggests that LC-related symptoms improve over time.[8] In a KCE (Belgian Healthcare Knowledge Centre) literature review, studies including those using outpatient data reported that between 3% and 36% (median value 32%) of patients still present with symptoms even after 3 months.[8]

Risk factors for LC include increasing age,[9–12] experiencing more than five symptoms during the first week of illness and the severity of illness during acute COVID-19 especially hospital admission.[10–12] In addition, pre-existing respiratory disease, higher body mass index,[10 11 13] the presence of comorbidities, female sex[11 12] and dyspnoea at 4–8 weeks.[10]

Military personnel in general, require physical and mental health usually greater than the civilian population during training or when deployed, as they may have to face harsh physical conditions (hostile climate, carrying heavy loads like ballistic protective gear) and diminished access to medical facilities.

Therefore, the objectives of this study are threefold: first, determine the prevalence of LC and the different clusters of symptoms in the Belgian Defence population while describing the range and severity of symptoms. Second, identify risk factors such as age, gender, blood type, body mass index (BMI), smoking habits (non-smoker, former-smoker, daily or occasional smoker), number of hours of exercise per week before infection and chronic diseases present before COVID-19 for LC. Third, assess the impact of LC on the quality of life (QoL) using the EuroQol 5 Dimension 5 Level (EQ-5D-5L) questionnaire.

METHODS

Procedures

On 20 September 2021, an online survey was sent via email to the work addresses of 2192 active Belgian Defence personnel who were known to have been SARS-CoV-2 PCR positive per the National Military Contact and tracing Centre (NMCC) between 17 August 2020 and 31 May 2021. Information including a letter detailing the study goals, procedures and an informed consent document were included (see online supplemental material). The data were collected during 3 weeks via the online survey platform MedSurveys and provided anonymously to the researchers by the data manager of the Directorate General Health & Well-being.

According to the sample size calculation,[14] 328 interviewees are needed for a statistically sufficiently large sample to achieve a 95% confidence level.

Variables and instruments

The online survey (see online supplemental material) consisted of three parts: a generic demographics and medical part, a specific COVID-19-related part and the EQ-5D-5L questionnaire as previously described by the EuroQol group,[15] valuing health-related QoL (HRQoL).

In the absence of international consensus, for the purposes of this study, LC was defined as the persistence of at least one symptom beyond 12 weeks after the onset of COVID-19 that cannot be explained by another diagnosis.

Statistical analysis

Analyses were performed with IBM SPSS V.25.0 (IBM, Armonk, New York, USA); the significance level for all analyses was set at an alpha of 0.05.

The study sample was first described (frequencies, means and SD) and compared with the target population using data from the NMCC.

Summary statistics then described the prevalence of LC and seven different clusters of LC presentation: chronic fatigue syndrome, cardiorespiratory, neuropsychiatric, dysautonomia, skin, musculo-articular and digestive cluster. Additionally, the most common symptoms during various time frames in the population were also described. The clusters of LC were based on a clinical categorisation of the symptoms (Table 1).

Table 1 Clusters of long COVID (LC)

Clusters of LC	Symptoms
Chronic fatigue	Fatigue or exhaustion
	Lack of energy
Cardiorespiratory	Shortness of breath or difficulty breathing
	Chest pain or tightness
	Cough
	Voice problems (hoarseness, loss of voice)
Neuropsychiatric	Loss of smell
	Loss of taste
	Headaches
	Speech problems (difficulty in pronouncing or finding words)
	Hearing problems
	Vision problems
	Concentration problem
	Insomnia
	Memory difficulties or loss
	Feeling of agitation and/or nervousness
	Mood swings
	Feeling down or depressed
	Stress
	Irritability
	Fear/Anxiety
	Libido problems
	Sadness
	Anger/Aggression
	Feeling of abandonment
	Euphoria
Dysautonomia	Sweating or hot flashes
	Urinary incontinence
	High temperature or fever >38°C
	Dry mouth
	Tingling and/or numbness of the skin
	Swelling (oedema)
	Swallowing problems (to swallow)
Cutaneous	Difficult to heal
	Dry, painful or itchy skin, rash
	Hair loss
Musculo-articular	Muscle pain and/or weakness
	Joint pains
Digestive	Abdominal pain
	Loss of appetite
	Nausea and/or vomiting
	Constipation and/or diarrhoea
	Gastric reflux (acidity)
	Weight loss
	Weight gain

LC risk factors

To determine risk factors related to the development of LC, we used binary logistic regression in the explanatory analysis. The independent variables were defined as age, sex, blood type, obesity at the time of infection (BMI ≥30), smoking habits, number of hours of exercise per week prior to infection, chronic disease comorbidity and medical operational category at the time of infection (A indicates medical fitness for all missions abroad, B temporary unfitness and C permanent unfitness. W (waiver) indicates medical fitness under certain conditions. O (overdue) means that the periodic assessment has expired and S (suspended) that the medical file is awaiting complementary information. Chronic diseases were only included in the regression model if at least 10 participants reported the presence of this disease. In a multivariate analysis, all independent variables were added to one model with the dependent variable being LC (yes/no) or a specific cluster of LC.

Impact of LC on QoL

The EQ-5D-5L questionnaire was used to measure the impact of LC on the QoL. All questions were scored for two different time points which included "how I felt before my COVID-19 infection" and "how I feel now" (both questions retrospective).

Five dependent variables were created (mobility, activities of daily living, self-care, anxiety/depression and pain/discomfort) and a distinction was made between an improved, neutral or a deteriorated state for each variable after COVID-19. The improved state was considered 'missing' because it occurred very rarely and an improvement of the health status was not expected after COVID-19. Thus, a binary variable was created; neutral/deteriorated.

The impact of LC on QoL was measured by binary logistic regression. The five variables described above were used as the dependent variable after controlling for the aforementioned independent variables.

Finally, a binary variable was created by taking the difference in health estimates out of a possible score of 100 before and after COVID-19. This number was then used to determine whether a higher deviation than the median value in the group occurred. A binary logistic regression was used to analyse which variables could be related to a higher deviation of the difference in health estimate before and after COVID-19. The independent variables were the different clusters of LC corrected for the aforementioned independent variables.

RESULTS

Response rate

A total of 34.7% replied and 718 questionnaires were fully completed, which is statistically large enough for a confidence level of 95%. Thirty-six incomplete questionnaires were not included. Compared with the overall defence target population, the study sample was significantly older (median 43 compared with 36 years) and contained significantly more women (12.53% compared with 9.40%), officers (21.32% compared with 12.64%) and non-commissioned officers (48.81% compared with 40.88%).

Descriptive statistics

Descriptive statistics of the study sample can be found in Table 2. In the fourth quarter of 2020 (second wave), 61.8% (n=444) of the participants tested positive, meaning their infection took place 7–10 months before the study; 3.5% (n=25) of the participants were infected earlier (August or September 2020) and 34.7% (n=249) were infected later (January 2021–May 2021).

Of the study participants, 62.12% reported no chronic diseases prior to their infection with COVID-19.

Mild-to-moderate (=non-hospitalised) COVID-19 was reported by 96.8% (n=695) of the participants, while 3.21% (n=23) were hospitalised of which 26% (n=6) needed admission to the intensive care unit.

Table 2 Descriptive statistics of the study sample

		% Sample
Gender	Male	87.33
	Female	12.53
Grade	Soldier	26.65
	Non-commissioned officer	48.81
	Officer	21.32
	Civil	3.23
Age	Mean (SD) in years	41.42 (11.09)
Function	Administrative	51.53
	Combat	14.90
	Navy (operational)	2.51
	Air force (operational)	2.09
	Medical supporting personnel (patient contact)	7.24
	Logistic (without contact combat)	10.58
	Logistic (with contact combat)	11.14
Symptoms	Yes	88.58
	No	11.42
Hospitalisation	No	96.80
	Yes, but no intensive care	2.37
	Yes, intensive care	0.84
BMI	<18.8	0.60
	18.5–25	38.90
	26–30	44.60
	>30	16.00
Sick leave	No (except isolation)	59.79
	<2 weeks	25.66
	2–4 weeks	13.23
	1–2 months	0.79
	2–3 months	0.53
	3–6 months	0.00
Chronic disease	No chronic condition	62.12
	Respiratory disease	7.24
	Heart or blood vessel disease	6.96
	Cutaneous disease	6.69
	Digestive disease	3.90
	Metabolic disease	3.48
	Locomotor disease	2.79
	Mental disease	1.67
	Blood or immunity disease	1.39
	Cancers	1.11
	Other*	2.65
Time of PCR positivity	August–September 2020	3.50
	October–December 2020	61.84
	January–May 2021	34.70
Hospitalisation	None	96.8
	Yes (normal unit)	2.37
	Yes (intensive care)	0.84

*Diseases including ear or vestibular system disease other than hearing impairment, genitourinary system disease, eye and adnexal disease other than refractive error, nervous system disease and infectious diseases.
BMI, body mass index.

Prevalence of LC

Among the 718 respondents, 340 (47.35%) people reported at least one persistent symptom lasting >3 months.

Most of the LC cases presented within a neuropsychiatric cluster (71.76%). Fatigue and lack of energy were reported in 57.65% of cases; a cardiorespiratory cluster was found in

45.29%; a dysautonomia cluster in 20%; a musculo-articular cluster in 24.71%; a cutaneous cluster in 8.53% and a digestive cluster in 30.88% of LC cases. Only one in five LC cases presented as a single cluster.

The 10 most frequent symptoms that were reported for >3 months were fatigue or exhaustion (24.23%), lack of energy (19.22%), breathing difficulties (19.08%), loss of smell (12.40%), muscle pain and/or weakness (9.75%), concentration problems (9.33%), loss of taste (8.64%), insomnia (8.64%), joint pain (7.38%) and memory problems (7.24%).

Explanatory analysis

In a multivariate analysis (Table 3), obesity increased the risk for LC (OR 2.225 (95% CI 1.334 to 3.711)) as well as respiratory diseases (OR 2.715 (95% CI 1.108 to 6.652)) and a history of a blood or immune system disorder (OR 12.345 (95% CI 1.068 to 142.677)). Physical activity of 3 hours per week or more decreases the odds for LC (OR 0.446 (95% CI 0.210 to 0.948)).

On a subanalysis examining associations between risk factors and clustered symptoms, obesity was significantly associated with the chronic fatigue cluster (OR 1.978 (95% CI 1.180 to 3.315)). With a BMI of 30 or above, the odds for a cardiorespiratory cluster of LC increased (OR 2.68 (95% CI 1.55 to 4.64)). Respiratory disease (OR 3.710 (95% CI 1.086 to 12.671)) and older age (OR 1.038 (95% CI 1.002 to 1.076)) increased the odds of developing a dysautonomia cluster.

Non-smokers were less likely to develop a cardiorespiratory cluster than daily smokers (OR 0.364 (95% CI 0.173 to 0.764)). Physical activity, including practising sport between 3 and 7 hours, or >7 hours per week reduced the odds of developing a neuropsychiatric cluster (OR 0.405 (95% CI 0.194 to 0.843) and OR 0.344 (95% CI 0.147 to 0.804), respectively).

Obesity (OR 3.216 (95% CI 1.626 to 6.247)), the presence of metabolic disease (OR 3.824 (95% CI 1.054 to 13.870)) and a haematological or immune system disease (OR 8.359 (95% CI 1.299 to 53.781)) were associated with the musculo-articular cluster of LC, while blood type O was associated with lower odds (OR 0.504 (95% CI 0.278 to 0.914)).

The odds of developing a digestive cluster of LC were increased among those with a history of digestive disease (OR 7.160 (95% CI 1.903 to 26.935)), respiratory disease (OR 4.302 (95% CI 1.219 to 15.185)) or obesity (OR 2.534 (95% CI 1.361 to 4.716)). The odds of developing a digestive cluster of LC decreased among those reporting a comorbid condition (ie, at least one existing chronic disease) (OR 0.229 (95% CI 0.065 to 0.812)).

Impact on QoL

The impact of LC on the QoL was measured using binary logistic regression (Table 4).

Mobility was negatively associated among those with LC reporting a cardiorespiratory cluster (OR 2.62 (95% CI 1.53 to 4.52)) of symptoms.

Deterioration in the activities of daily living was observed among those with LC reporting three different clusters of symptoms: chronic fatigue cluster (OR 4.11 (95% CI 2.18 to 7.76)), cardiorespiratory cluster (OR 2.66 (95% CI 1.48 to 4.79)) and autonomic nervous system cluster (OR 2.33 (95% CI 1.11 to 4.92)). For former or non-smokers, the impact seems to be smaller compared with smokers (OR 0.23 (95% CI 0.08 to 0.64) and OR 0.37 (95% CI 0.16 to 0.88), respectively).

Anxiety or depression was associated with four clusters of LC: chronic fatigue cluster (OR 4.15 (95% CI 2.10 to 8.17)),

Table 3 Significant (p<0.05) p values of the binary logistic regression analysis of long COVID and the clusters of long COVID (without cutaneous cluster n<30) with confounding factors and their ORs

	Long COVID		Fatigue		Cardiorespiratory		Neuropsychiatric		Dysautonomia		Musculo-articular		Digestive	
	N=340	OR	N=196	OR	N=154	OR	N=244	OR	N=68	OR	N=84	OR	N=105	OR
	P value	95% CI	P value	95% CI	P value	95% CI	P value	95% CI	P value	95% CI	P value	95% CI	P value	95% CI
Age	0.85		0.33		0.60		0.60		0.04	1.038 (1.002 to 1.076)	0.44		0.36	
Blood group	0.44		0.37		0.64		0.18		0.72		0.07		0.13	
O	0.26		0.17		0.42		0.07		0.75		0.02	0.50 (0.28 to 0.91)	0.95	
Obesity	0.002	2.23 (1.33 to 3.71)	0.01	1.98 (1.18 to 3.32)	<0.001	2.68 (1.55 to 4.64)	0.34		0.67		<0.001	3.22 (1.63 to 6.25)	0.003	2.53 (1.36 to 4.72)
Smoking	0.82		0.91		0.05		0.77		0.78		0.63		0.69	
Non-smoker	0.53		0.47		0.01	0.36 (0.17 to 0.75)	0.67		0.57		0.58		0.38	
Sports before COVID-19	0.18		0.37		0.44		0.05		0.39		0.92		0.52	
<3 hours	0.10		0.21		0.49		0.12		0.43		0.74		0.93	
3–7 hours	0.04	0.45 (0.21 to 0.95)	0.15		0.42		0.02	0.405 (0.194 to 0.843)	0.75		0.53		0.35	
>7 hours	0.05	0.43 (0.18 to 0.99)	0.08		0.74		0.01	0.344 (0.147 to 0.804)	0.59		0.74		0.60	
Comorbidity	0.06		0.92		0.15		0.78		0.10		0.40		0.02	0.23 (0.07 to 0.81)
Respiratory disease	0.03	2.72 (1.11 to 6.65)	0.26		0.35	0.25 (0.07 to 0.99)	0.27		0.04	3.710 (1.086 to 12.671)	0.11		0.02	4.30 (1.22 to 15.19)
Digestive disease	0.18		0.38		0.05		0.53		0.74		0.77		0.004	7.16 (1.90 to 26.94)
Blood or immunity disease	0.04	12.35 (1.07 to 142.68)	0.15		0.38		0.23		0.55		0.03	8.36 (1.3 to 53.78)	0.21	
Metabolic disease	0.46		0.56		0.27		0.33		0.44		0.04	3.82 (1.05 to 13.87)	0.09	

Table 4 Significant (p<0.05) p values of the binary logistic regression analysis of four domains of QoL and the clusters of long COVID and their ORs

	Mobility		Activities of daily living		Anxiety/Depression		Pain/Discomfort		Health estimate QoL	
N=(detoriated/neutral/improved)		134/577/6	118/594/5		117/597/3		157/553/7		281/436/0	
	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)
Gender									0.013	2.29 (1.19 to 4.39)
Long COVID							0.003	3.33 (1.50 to 7.38)		
Fatigue cluster			<0.001	4.11 (2.18 to 7.76)	<0.001	4.15 (2.10 to 8.17)	0.001	2.48 (1.44 to 4.27)	<0.001	3.08 (1.79 to 5.30)
Cardiorespiratory cluster	<0.001	2.62 (1.53 to 4.52)	0.001	2.66 (1.48 to 4.79)					<0.001	2.91 (1.61 to 5.24)
Neuropsychiatric cluster					<0.001	7.13 (2.95 to 17.23)				
Dysautonomia cluster			0.026	2.33 (1.11 to 4.92)			0.007	2.72 (1.32 to 5.63)		
Cutaneaus cluster					0.012	5.56 (1.46 to 21.12)				
Digestive cluster					<0.001	3.05 (1.61 to 5.79)			<0.001	3.39 (1.68 to 6.82)
Musculo-articular cluster							<0.001	3.18 (1.66 to 6.07)	<0.001	5.39 (2.14 to 13.53)
Smoking			0.046	/						
Former smoker			0.005	0.23 (0.08 to 0.64)						
Non-smoker			0.025	0.37 (0.16 to 0.88)						
Sports before COVID-19			0.006	/					0.023	
>7 hours									0.040	2.54 (1.05 to 6.18)
Disease cardiovascular									0.025	0.31 (0.11 to 0.86)
Locomotor disease									0.035	0.23 (0.06 to 0.90)
Digestive disease							0.044	0.18 (0.03 to 0.96)		
Blood or immunity disease							0.039	0.09 (0.01 to 0.89)		

The fifth cluster (self-care) was not impacted and thus not included in the table.
The binary outcome of the four domains of quality of life was defined as a detoriated or a neutral state after the infection with COVID-19.
QoL, quality of life.

neuropsychiatric cluster (OR 7.13 (95% CI 2.95 to 17.23)), cutaneous cluster (OR 5.56 (95% CI 1.46 to 21.12)) and digestive cluster (OR 3.05 (95% CI 1.61 to 5.79)).

Increased levels within the pain spectrum were associated with LC in general (OR 3.33 (95% CI 1.50 to 7.38)) and more specifically within three clusters: chronic fatigue cluster (OR 2.48 (95% CI 1.44 to 4.27)), dysautonomia cluster (OR 2.72 (95% CI 1.32 to 5.63)) and musculo-articular cluster (OR 3.18 (95% CI 1.66 to 6.07)). For people reporting previous digestive or immune/blood disorders, the effect of LC on pain was less when compared with people who did not report any chronic conditions (OR 0.18 (95% CI 0.03 to 0.96) and OR 0.09 (95% CI 0.01 to 0.89), respectively).

No variables were associated with a deterioration in the self-care dimension.

After COVID-19, a significantly greater decrease in the median QoL score was observed in the LC group compared with the group without LC (11 vs 4 points decrease, respectively). A change in the health status estimate (before and after COVID-19) is influenced by the following four clusters of LC: fatigue (OR 3.08 (95% CI 1.79 to 5.30)), cardiorespiratory (OR 2.91 (95% CI 1.61 to 5.24)), digestive (OR 3.39 (95% CI 1.68 to 6.82)) and musculo-articular cluster (OR 5.39 (95% CI 2.14 to 13.53)). We also noted a greater decrease in the QoL for women compared with men (OR 2.29 (95% CI 1.19 to 4.39)). People who reported >7 hours of sports per week before their infection would report a higher deterioration of their estimated health compared with people who did not exercise (OR 2.54 (95% CI 1.05 to 6.18)). Patients with an existing cardiovascular disease and locomotor disease reported a smaller deterioration after a COVID-19 infection when compared with those without any cardiac or locomotor disease (OR 0.31 (95% CI 0.11 to 0.86) and OR 0.23 (95% CI 0.06 to 0.90), respectively).

DISCUSSION

Prevalence of LC

In the survey, 47.35% of participants reported at least one symptom lasting over 3 months after initial SARS-CoV-2 infection, which is similar to the prevalence of 47% found in the COVIMPACT study by Sciensano, within the Belgian population.[16] Fatigue or exhaustion was the most prevalent LC symptom in both studies.

In the absence of a broad scientific consensus regarding classification and underlying pathological mechanisms of LC, we decided to reduce the myriad COVID-19-related symptoms into seven clinical clusters. This classification is primarily based on symptomatology and body systems, not on the presence of shared underlying pathological mechanisms. We have deliberately grouped neurological and psychiatric symptoms into one cluster since the mechanism(s) explaining these symptoms is unknown. Grouping LC symptoms in this manner is less synoptic than the King's College classification which only uses three predominant profiles which are not validated and therefore not used to guide clinical practice.[17] On the other hand, it created the opportunity to bring clinical nuance and further clarify clinical presentation that could be used to target treatment approaches.

The most prevalent LC cluster was the neuropsychiatric cluster (71.76%). This could be partially explained by pathogen factors related to the Alpha and Delta variants. SARS-CoV-2 variants appeared in Belgium beginning in December 2020. Likely many of the participants responding to the survey were infected by the Alpha or Delta variant in addition to the original strain. Some evidence suggests that these variants induce more neuropsychiatric symptoms than the original strain.[18] Furthermore, neurological symptoms are more frequently reported in case of infections with the Alpha and Delta variants, compared with the original strain.[17] Concurrent stressors related to the pandemic such as social isolation, stress and uncertainty can also contribute to the symptomatology and drive a higher prevalence of neuropsychiatric LC[19] cluster-related symptoms.

LC explanatory factors

We identified obesity, immune and blood disorders and respiratory disease as important risk factors associated with LC and were associated with multiple symptom clusters. Obesity was identified as a risk factor for all LC clusters except the neuropsychiatric and dysautonomia cluster.

Increased BMI or obesity, and airway disease such as asthma are risk factors for LC in other studies as well.[13 20] Older age was found to be a risk factor in other studies including a systematic review of the literature that found an age between 40 and 49 years is associated with developing LC.[21] Additionally, in another systematic review the 35–69 years age group seemed to be the most affected by LC.[8] However, in our study age was only found to be associated with the dysautonomia cluster.

The association between obesity and LC might be expected because of the multisystemic changes associated with obesity.[22] LC in general and the neuropsychiatric LC cluster were positively impacted by fitness, specifically, the amount of athletic practice before the COVID-19 infection. This effect could be related to a healthier weight and the presence of good physical and mental health.[20] Female gender and mental disease have been found to be risk factors in other studies, but this was not observed in our study.[23]

The association of the musculo-articular cluster to existing blood or immune system disorders could be related to the production of autoantibodies. In a study by Richter *et al*[24] of patients with COVID-19 receiving intensive care treatment, SARS-CoV-2 infection is associated with the production of a limited profile of autoantibodies specific to skin, muscle, skeletal and cardiac tissues.

We did not identify an effect of medical operational categories on the development of LC. This is in contrast to recent unpublished work in the UK military that identified 20%–30% of those who developed LC were not fully medically deployable. This could be due to the fact that the medical operational category is not necessarily a reflection of the general health of the personnel but rather an administrative state demonstrating the execution of medical screenings, dental evaluation and vaccination status. This may be different in the UK, where predeployment screenings can be more sensitive to LC symptoms.

Quality of life

The EQ-5D-5L questionnaire data identified a greater negative impact in at least one of the LC clusters compared with the group without LC. Only the self-care dimension was not affected by any of the LC clusters.

Our study detected a significant decrease of 11 points on the EQ Visual Analogue Scale in the LC group. In comparison, a decrease of 10.4 points in the QoL score was observed in the COVIMPACT study by Sciensano[16] and of 24 points in the KCE LC patient needs study.[8]

Treatment

The current study did not explore the effect of possible treatments on LC. However, based on literature, military personnel exposed to high volume/intensity physical exercise, or hospitalised during acute illness, may benefit from cardiopulmonary monitoring and appropriate rehabilitation beyond 5 months[25] and should be medically assessed before returning to work.[26] Chronic fatigue patients could consider experimental hyperbaric oxygen treatment (HBOT), as suggested by a small-scale study in the UK, showing positive results after 10 sessions.[27] A HBOT study was started in the Belgian Defence targeting all LC clusters.

Study limitations

Our study does not consider the effect of vaccination against SARS-CoV-2 on LC development, despite its proven effectiveness in other studies[28] and the fact vaccination is mandatory in deployable personnel and healthcare workers in Belgium. However, 40% of our sample was infected in October 2020 (at the peak of the second wave in Belgium) and 62% before January 2021, which means the vaccination level in our sample was likely to be low. Recent studies show positive effects of vaccination on the occurrence of prolonged symptoms (beyond 4 weeks) after the second dose.[28] In another study with at least two doses, 7 of the 10 most common LC symptoms were reduced by 54%–82%.[29]

Approximately two-thirds of the participants in our study responded to the online questionnaire 7–8 months after their initial infection. This relatively long interval could create a memory or recall bias regarding the duration of symptoms. In addition, selection bias may have appeared in which those who continued to have symptoms are more likely to reply to the survey than those who do not. Due to the self-reporting of the symptoms and their duration, the prevalence of LC in our population may be an overestimation.

Because of the small numbers of some pre-existing conditions (n<10), we could not analyse their relation with the development of LC.

Conclusion

The prevalence of LC in the Belgian active defence population (civil and military) is similar to the prevalence found in the Belgian population[16] and the QoL impact is substantial. Regardless of initial disease severity or SARS-CoV-2 laboratory confirmation, patients with LC would likely benefit from multidisciplinary rehabilitation assessment, especially when addressing the most prevalent symptoms of shortness of breath, fatigue and mood disturbance.[30]

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