

Patients with persistent symptoms after COVID-19 attending a multidisciplinary evaluation: Characteristics, medical conclusions, and satisfaction

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ARTICLE INFO

Keywords:

Long COVID

Persistent symptoms

Functional somatic disorder

Multidisciplinary care

ABSTRACT

Objective: Among patients attending a multidisciplinary day-hospital program for persistent symptoms after COVID-19, we aimed i) to describe their characteristics ii) to present the medical conclusions (diagnoses and recommendations) and iii) to assess the patients' satisfaction and its correlates.

Methods: For this retrospective chart review study, frequent symptoms were systematically assessed. Standardized questionnaires explored fatigue (Pichot scale), physical activity (Ricci & Gagnon scale), health-related quality of life (Short-Form Health Survey), anxiety and depressive symptoms (Hospital Anxiety and Depression scale) and associated psychological burden (Somatic-Symptom-Disorder B criteria Scale). Medical record conclusions were collected and a satisfaction survey was performed at 3-months follow-up.

Results: Among 286 consecutive patients (median age: 44 years; 70% women), the most frequent symptoms were fatigue (86%), breathlessness (65%), joint/muscular pain (61%) and cognitive dysfunction (58%), with a median duration of 429 days (Inter-quartile range (IQR): 216–624). Questionnaires revealed low levels of physical activity and quality of life, and high levels of fatigue, anxiety, depression, and psychological burden, with 32% and 23% meeting the diagnostic criteria for a depressive or anxiety disorder, respectively. Positive arguments for a functional somatic disorder were found in 76% of patients, including 96% with no abnormal clinical or test findings that may explain the symptoms. Physical activity rehabilitation was recommended for 91% of patients. Patients' median satisfaction was 8/10 (IQR: 6–9).

Conclusion: Most patients attending this program presented with long-lasting symptoms and severe quality of life impairment, received a diagnosis of functional somatic disorder, and reported high levels of satisfaction regarding the program.

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1. Introduction

Many patients report persistent symptoms following coronavirus disease 2019 (COVID-19), even after a mild infection, with up to 10% at 12 months [1,2]. Moreover, these manifestations are frequently disabling and can impair quality of life. This clinical situation, frequently referred to as 'long COVID', is a public health issue. Clinicians have been urged to create dedicated care settings for these patients and guidelines have been issued advocating for a comprehensive evaluation [3–5] that takes into account the clinical heterogeneity of this condition, encompassing both mental health issues and physical deconditioning.

According to the World Health Organization, the 'Post-COVID-19 Condition' is defined as the presence of any symptom occurring within three months from the onset of the infection and persisting for at least two months, as long as it has an impact on everyday functioning and cannot be explained by another diagnosis [6]. A frequent clinical feature is the contrast between the severity of the symptoms and the absence of pathological findings on the physical examination and routine tests that may fully explain the symptoms presented [7–11]. However, the lack of specificity of the symptoms (e.g., fatigue, shortness of breath, pain, or cognitive dysfunction) and the default attribution to COVID-19 result in great clinical heterogeneity [12,13], warranting a cautious and comprehensive medical assessment.

Patients with Post-COVID-19 condition also present with high prevalence of depression and anxiety [14]. This association might be bidirectional. First, although it has been suggested that anxiety and depressive symptoms might result from the infection itself [15], they may also result from the impact of persistent symptoms on daily life, uncertainty about their evolution, and the associated stigma [16]. Specifically, the psychological burden associated with persistent symptoms might be consistent with a diagnosis of a 'somatic symptom disorder' as defined in the DSM-5 [7,17,18]. On the other hand, psychological distress is also a risk factor of persistent symptoms after COVID-19 infection [19–23]. In addition, psychological mechanisms, such as health beliefs and their influence on perception and health behaviors can influence the persistence of some symptoms [8,24–27]. Combined with the aforementioned absence of pathological findings on physical examination and routine tests that may fully explain the symptoms [7–11], these characteristics suggest that some patients with post-COVID-19 condition may present with both positive arguments (i.e., cognitive and behavioral mechanisms potentially involved in the maintenance of physical symptoms; see below) and negative arguments (i.e., absence of clinical or paraclinical pathological features that may fully explain the symptoms) in favor of a diagnosis of functional somatic disorder. Functional somatic disorders are indeed defined by persistent symptoms that are not or no longer explained by a dysfunction of the organ they point to [21,24,28]. Therefore, a comprehensive psychiatric assessment is warranted to search for both psychiatric complications and psychological risk factors of long COVID.

Patients with post-COVID-19 condition also frequently describe a dramatic reduction of physical activity. Reduced physical activity, particularly in the context of strict isolation at home during the initial phase of the infection, can provoke a physical "deconditioning spiral" that perpetuates the functional impairment [29,30]. Therefore, a precise assessment of physical condition and exercise habits can guide appropriate rehabilitation that may improve symptoms and quality of life [31].

In accordance with these elements and available guidelines [3–5], a multidisciplinary day-hospital program dedicated to patients with post-COVID-19 condition has been implemented in a university hospital since July 2021 in Paris, France. The aim of this retrospective chart review observational study was i) to describe the clinical characteristics of patients attending this program in its first year, ii) to present the medical conclusions (diagnoses and recommendations), and iii) to assess the patients' satisfaction and its correlates.

2. Methods

2.1. Patients

The CASPer-COVID (Circuit Ambulatoire de prise en charge des Symptômes Persistants après un épisode de COVID-19) program is referenced by the health regional agency of the Paris area for managing post-COVID-19 condition. Patients are self-referred or referred by their general practitioners. They are required to fill out a medical questionnaire including features of the initial COVID episode, current persistent symptoms, and previous medical investigations and their conclusions. As recommended by French, UK and US guidelines [3–5], the required explorations include a set of systematic laboratory tests, and complementary tests guided by the presented symptoms. A detailed description of the systematic medical work-up required and complementary explorations depending on the presented symptoms is available as supplementary material [3–5]. In the present analysis, we included all patients who attended the CASPer-COVID program from July 8th, 2021 to September 6th, 2022 due to symptoms persisting for >2 months after a documented or self-reported infection with SARS-CoV-2.

After confirming that the intended research did not involve human subject as defined by the French law n°2012–300 of March 5, 2012, regarding research involving human subjects, the project received favorable approval on November 18, 2022, by the Research Ethics Committee of the APHP-Centre University Hospital group. As this is a retrospective chart review observational study, written consent was not required.

2.2. Evaluation

The CASPer-COVID program is a multidisciplinary day-hospital evaluation.

Before admission, a physician (BR or KX) carefully examines the medical records and the filled medical questionnaire, and any needed supplemental biological tests or imaging are planned in order to have the results on the day of hospitalization. Patients are also invited to fill out other questionnaires regarding fatigue (Pichot scale [32]: eight item scoring 0–4, a score > 22 indicating high levels of fatigue), physical activity (Ricci & Gagnon scale [33]: nine items scoring 1–5, a score < 18 indicating low physical activity), health-related quality of life (36-Item Short-Form Health survey questionnaire [34] (SF-36), yielding a physical component summary and a mental component summary with higher scores (from 0 to 100) indicating higher levels of quality of life), depressive and anxiety symptoms (Hospital Anxiety and Depression Scale (HAD-S): 14 items scoring 0–3, yielding two subscores with a score ≥ 8 indicating high levels of anxiety or depression) [35], and psychological burden associated with the persistent symptoms (Somatic Symptom Disorder-B criteria Scale (SSD-12): 12 items scoring 0–4 designed to assess the cognitive, affective and behavioral features of the DSM-5 Somatic symptom disorder B criteria, with a score ≥ 23 indicating high levels of psychological burden) [36].

During the day-hospital evaluation, patients undergo three consecutive one-hour consultations with an internist or infectious disease specialist, a psychiatrist, and an adapted physical activity specialist. The physical examination searches for sequelae of the initial COVID-19 infection and other comorbid conditions that may account for the persistent symptoms. The psychiatrist looks for comorbid psychiatric disorders and cognitive and behavioral mechanisms potentially involved in the maintenance of physical symptoms such as classical conditioning, focused attention on bodily functioning, catastrophizing, avoidance of symptoms and intolerance to uncertainty [37,38]. Should such mechanisms be identified, a brief psychoeducational intervention regarding their potential role is proposed during the consultation. This psychoeducational intervention consists in presenting the different potential cognitive and behavioral mechanisms as listed above, depending on the patient's experience and consistent with his or her narrative. This

presentation builds on examples from scientific literature but also from everyday life, in which these mechanisms are involved, in order to facilitate the physician-patient relationship and to promote therapeutic alliance [39]. Third, an adapted physical activity specialist evaluates the patient's physical condition and exercise habits and perform standardized physical tests evaluating cardiorespiratory deconditioning and muscle strength deficiency compared to age-related standards. After a multidisciplinary consultation meeting between the three specialists, the patients and their general practitioner receive personalized recommendations as needed, including: complementary medical explorations, physical activity rehabilitation program, referral to a psychiatrist or psychologist, cognitive remediation, prescription of psychotropic drugs.

2.3. Data collection

The following variables were systematically extracted from the medical record: age and gender, characteristics of the acute episode of COVID-19 and its management (i.e., hospitalization, need for oxygen therapy, or intensive care unit), persistent symptoms and their duration as well as sickness absence related to symptoms and their evolution, and responses to the above-mentioned questionnaires. We also collected the conclusions of this day-hospital evaluation, i.e., the presence of abnormal clinical findings or test results, the need for further medical examination or specialized consultation, the presence of a depressive or anxiety disorder, the presence of cognitive and behavioral mechanisms potentially involved in the maintenance of physical symptoms, and the recommendations regarding physical activity (i.e., no need for physical rehabilitation, self-rehabilitation with recommended exercises, rehabilitation in a specific certified sport center, or hospital rehabilitation program).

Finally, should abnormal clinical findings or test results be mentioned, medical records were carefully reviewed by senior physicians (CG, KX, BR) to assess whether these findings may account at least partially for the persistent symptoms. The diagnosis of "functional somatic disorder" was therefore based on a combination of both positive arguments (i.e., the presence of potential cognitive and behavioral mechanisms as listed above) and negative arguments (i.e., the absence of abnormal clinical findings or test results potentially explaining the symptoms).

A satisfaction survey was performed at 3-month follow-up. An e-mail was sent to patients to ask whether they would agree to be contacted by phone for a satisfaction survey regarding the program. During this telephone call, we collected i) their overall degree of satisfaction regarding the program, ii) the perceived effectiveness of the program, and iii) whether they would recommend other patients to attend this program. For each of these three components, participants were asked to rate their experience from a scale ranging from 0 to 10, 0 being the lowest level of satisfaction and 10 being the highest.

2.4. Statistical analysis

Descriptive analyses used percentages for categorical variables and median and interquartile ranges for continuous variables.

The associations between the presence of positive arguments for a functional somatic disorder and i) the absence of abnormal clinical findings or test results potentially explaining the symptoms and ii) a SSD-12 score ≥ 23 suggesting the presence of DSM-5 diagnosis criteria of a somatic symptom disorder [36] as well as the association between a diagnosis of functional somatic disorder (combining both positive and negative arguments) and a diagnosis of depression were examined with Pearson chi-square tests.

The unadjusted associations between the diagnosis of functional somatic disorder and satisfaction measures were examined with Kruskal-Wallis tests. To identify the factors associated with each satisfaction measure, we first conducted unadjusted linear regression analyses for age, gender, symptoms presented, their duration, SF-36 mental and

physical component scores, and medical conclusions. Then we computed multivariable linear regression models adjusting for age, gender, medical conclusions and variables that were associated with $p < 0.1$ in unadjusted analysis. The characteristics of patients who completed the satisfaction survey were compared to the characteristics of those who did not with Pearson's chi square tests for categorical variables, and Kruskal Wallis' tests for continuous variables.

All data analyses were performed using Stata 15.0 (StataCorp, College Station, TX). The significance threshold was set at two-tailed $p < 0.05$.

3. Results

3.1. Patients

On September 6th, 2022, a total of 301 patients attended the CASPer-COVID program. Among them, 15 were referred for persistent symptoms not attributed to COVID-19 and were excluded from the analysis. Among the 286 patients consulting for persistent symptoms after a SARS-CoV-2 infection, 201 were women (70.3%) and median age was 44 years (Interquartile range [IqR]: 34–55).

3.2. Persistent symptoms

Figure 1 presents the most frequent self-reported persistent symptoms. The most frequent symptoms were fatigue (85.6%), followed by shortness of breath (64.9%), joint or muscle pain (60.5%) and cognitive dysfunction (57.6%). Persistent symptoms were lasting for a median duration of 428.5 days (IqR: 216–624).

3.3. Clinical features

Table 1 reports the characteristics of the patients, including the severity of the acute episode, the professional impact, the results of the self-administered questionnaires, the medical conclusions (including psychiatric diagnoses) and recommendations.

A total of 35 patients (12.7%) were hospitalized, indicating severe COVID-19 episode, and 150 (69.4%) had sickness absence for persistent symptoms, with a median duration [IqR] of 5 [2–9] months.

Questionnaires revealed low levels of physical activity and health-related quality of life, and high levels of fatigue, anxiety, depression and psychological burden, with 31.7% and 22.5% meeting the diagnostic criteria for a depressive or anxiety disorder.

After a comprehensive examination, further medical explorations or tests were recommended in 105 patients (37.6%), while 250 (91.2%) had a recommendation for some kind of physical activity rehabilitation.

Cognitive and behavioral features that may contribute to the maintenance of physical symptoms (i.e., classical conditioning, focused attention on bodily functioning, catastrophizing, avoidance of symptoms and intolerance to uncertainty) were identified in 75.5% of patients after clinical evaluation and were considered as positive arguments in favor of a diagnosis of functional somatic disorder. Among these patients, 95.6% did not present any abnormal clinical findings or test results that could potentially explain the symptoms (Table 2). Therefore, a diagnosis of functional somatic disorder based on positive and negative arguments was retained for 72.2% of the patients after the multidisciplinary assessment.

In addition, among patients with positive arguments in favor of a diagnosis of functional somatic disorder, only 73.8% had an SSD-12 score ≥ 23 (Table 3). Patients with a diagnosis of functional somatic disorder had similar rates of major depression (32.8%) and anxiety disorders (25.0%) than in the whole sample, with no significant difference compared to those without ($\chi^2 = 0.24$, $p = 0.63$ and $\chi^2 = 2.22$, $p = 0.14$ respectively; Table 4). Therefore, there was no significant difference concerning the proportion of patients with a diagnosis of functional somatic disorder between those with and without a diagnosis of major

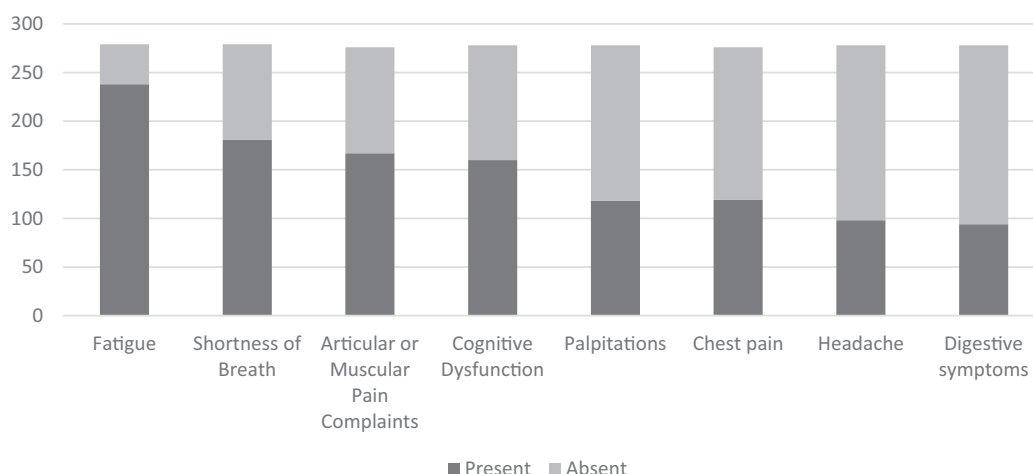


Fig. 1. Self-reported persistent symptoms.

Table 1
Characteristics of the population.

ACUTE COVID-19 EPISODE SEVERITY (n = 276)	n	%
Hospitalization	35	12.7
Oxygen therapy	13	4.7
Admission in intensive care unit	9	3.3
PROFESSIONAL IMPACT		
Sickness absence among workers (n = 216) (n, %)	150	69.4
Duration of sickness absence in months (n = 149) (median, IqR)	5	2–9
QUESTIONNAIRES		
	median	IqR
Fatigue: Pichot scale score (n = 261)	23	18–27
Physical activity: Ricci and Gagnon scale score (n = 236)	15	10–25
Quality of life: SF-36 score (physical) (n = 229)	39	32–49
Quality of life: SF-36 score (mental) (n = 229)	45	33–59
Anxiety: HAD-A score (n = 254)	9	5–12
Depression: HAD-D score (n = 256)	8	5–11
Persistent symptom associated burden: SSD-12 score (n = 259)	27	21–33
MEDICAL CONCLUSIONS		
	n	%
Depressive disorder (n = 271)	86	31.7
Anxiety disorder (n = 271)	61	22.5
Positive arguments for functional somatic disorder (n = 273)	206	75.5
Clinical or paraclinical abnormality potentially explaining the presented symptoms (n=278)	26	9.4
Need for further medical explorations of tests (n = 277)	105	37.6
PHYSICAL ACTIVITY RECOMMENDATION (N = 274)		
	n	%
No rehabilitation	24	8.8
Self-Rehabilitation with exercise program	111	40.5
Rehabilitation in ambulatory structure	69	25.2
Hospital rehabilitation program	62	22.6

HAD-A: Hospital Anxiety and Depression-Anxiety subscale; HAD-D: Hospital Anxiety and Depression-Depression subscale; SSD-12: Somatic symptom disorder B criteria scale; SF-36: Short-Form 36.

depression ($\chi^2 = 0.24$, $p = 0.63$).

3.4. Satisfaction

A total of 140 patients responded to our invitation to be contacted for the satisfaction survey at 3-month follow-up (49.0% of the whole sample). Median [IqR] rating for overall satisfaction, perceived effectiveness, and level of recommendation to other patients were 8 [6–9], 7 [4–9] and 9 [6–10], respectively. Among the subgroup of 81 patients who received a diagnosis of functional somatic disorder, satisfaction results were similar: 8 [6–10], 7 [3–10] and 9 [6–10], with no

Table 2
Clinical or paraclinical abnormalities among patients with or without positive arguments for a functional somatic disorder.

		No	Yes	Total
Positive arguments for a functional somatic disorder	No	50	17	67
	Yes	197	8	205
	Total	247	25	272

Table 3
Patients with a SSD-12-score ≥ 23 among patients with or without positive arguments for a functional disorder at clinical evaluation.

		SSD-12 score ≥ 23		
Positive arguments for a functional somatic disorder	No	24	36	60
	Yes	50	141	191
	Total	74	177	251

SSD-12: Somatic Symptom Disorder B criteria scale.

Table 4
Diagnosis of major depression among patients with a diagnosis of functional somatic disorder.

		Diagnosis of major depression		
Diagnosis of functional somatic disorder (combining positive and negative arguments)	No	52	22	74
	Yes	131	64	195
	Total	183	86	269

significant difference compared to those who did not (All $p > 0.27$ for Kruskal Wallis' tests).

Unadjusted regression models did not identify any statistically significant association between the three satisfaction measures (i.e., overall satisfaction, perceived effectiveness, and level of recommendation to other patients) and the presence of the different persistent symptoms or their duration. Concerning health-related quality of life, the only

association for which a $p < 0.1$ was found was between the level of recommendation to other patients and the SF-36 physical component score ($\beta = -0.04$; $p = 0.07$), which was thus included in the multivariable regression analysis.

In multivariable regression analyses, higher age, male gender, and having a clinical or paraclinical abnormality potentially explaining the symptoms were associated with higher levels of overall satisfaction, but not with the level of perceived effectiveness or estimated level of recommendation to other patients despite similar trends (Table 5). Apart from the latter association, medical conclusions were not associated with differences in satisfaction measures.

Patients who participated in the satisfaction survey did not statistically differ from those who did not participate regarding gender, health-related quality of life, or medical conclusions. The only statistically significant differences were a slight difference regarding median age (46 years for respondents (IqR 36–55) and 42 years for non-respondents (IqR 31–52); $p = 0.047$ for Kruskal Wallis test) and a more important proportion of patients with palpitations among respondents ($\chi^2 = 4.18$; $p = 0.04$) (supplementary material 2).

4. Discussion

We report the characteristics of 286 consecutive patients attending a multidisciplinary day-hospital evaluation program dedicated to the assessment and management of persistent symptoms after a SARS-CoV-2 infection. The most frequent persistent symptoms were fatigue, shortness of breath, pain complaints and cognitive complaints, consistent with the literature [12,13,40,41]. The burden of these persistent symptoms was heavy in our population, as indicated by the median duration of more than one year, the low scores of health-related quality of life, and frequent sickness absences lasting for several months in most cases. Poor mental health was also frequently observed with major depression and anxiety disorder in almost one third and one quarter of the patients, respectively. A major finding of our study is that most of them presented with both positive and negative arguments in favor of a diagnosis of functional somatic disorder, that is from persistent and debilitating symptoms that are no longer explained by a dysfunction of the organ they point to [28].

Specifically, three quarters of these patients presented with positive arguments in favor of a diagnosis of functional somatic disorder, including a history of symptoms consistent with the role of classical conditioning, focused attention on bodily functioning, catastrophizing, avoidance of symptoms and intolerance to uncertainty. Furthermore, despite a comprehensive medical workup, the vast majority of them did not exhibit any abnormal clinical findings or test results that may account for the persistent symptoms. Some patients did have a

recommendation for further medical explorations or tests prescribed after the multidisciplinary consultation. Nevertheless, these medical explorations may not have necessarily concerned the diagnosis underlying the presented symptoms, so that their results would not have changed the medical conclusions. The diagnosis of functional somatic disorder was thus retained in 72.2% of all patients. A small proportion of patients exhibiting positive arguments in favor of a diagnosis of functional somatic disorder nonetheless presented with abnormal clinical findings or test results potentially explaining at least some of their persistent symptoms. This situation is compatible with a diagnosis of somatic symptom disorder according to the DSM-5 criteria. Of note, the identification of positive arguments in favor of a diagnosis of functional somatic disorder only partially overlap with the presence of a high SSD-12 score. This is indeed consistent with the fact that the SSD-12 was designed to assess the cognitive, affective and behavioral features of the DSM-5 Somatic symptom disorder B criteria, which do not encompass some potential mechanisms of functional somatic disorders (e.g., avoidance of symptoms), while including some aspects of the associated psychological burden regardless of potential mechanisms (e.g., impaired concentration) [36].

Although we based the diagnosis of functional somatic disorder on both positive and negative arguments [28], some patients may exhibit symptoms of heterogeneous origin. For instance, persistent symptoms after a COVID-19 may result from various mechanisms [24,27,42]: sequelae of the initial episode, ongoing biological disturbances persisting beyond viral clearance (e.g., persistent inflammation or dysimmunity), classical conditioning leading to functional symptoms beyond lesions healing, focused attention toward bodily sensations leading to lower threshold of perception, excess attribution of any otherwise unexplained symptom to a recent episode of COVID-19, physical and cognitive symptoms of depression or anxiety, poor tolerance of physical activity due to physical deconditioning, etc. Although between-individual heterogeneity has been highlighted as challenging our ability to understand long COVID, within-individual heterogeneity is likely to be at least as challenging. From a clinical point of view, these potential mechanisms should not be considered as mutually exclusive, nor even independent. For instance, physical triggers such as acute infection have been shown to interact with cognitive and behavioral mechanisms in the onset of functional somatic disorder, thus precluding any dualistic approach [24,27]. A typical example is how psychological distress may influence the risk of developing an irritable bowel syndrome after an episode of acute gastro enteritis [43].

Perhaps surprisingly, patients with and without a diagnosis of functional somatic disorder had similar rates of depression and anxiety, highlighting the fact that functional somatic disorders should not be assimilated to physical symptoms of depression or anxiety, which may

Table 5

Variables associated with satisfaction scores in multivariable linear regression models ($n = 123$).

	Overall satisfaction			Perceived effectiveness			Level of recommendation		
	B	95% CI	p	B	95% CI	p	B	95% CI	p
Age (per year)	0.05	0.01; 0.09	0.01	0.04	-0.01; 0.09	0.14	0.04	-0.02; 0.09	0.20
Gender (women)	-1.13	-2.10; -0.15	0.02	-0.87	-2.15; 0.40	0.18	-1.46	-2.95; 0.03	0.055
Diagnostic conclusions									
Depressive disorder	0.52	-0.46; 1.49	0.30	0.19	-1.12; 1.49	0.77	0.90	-0.55; 2.35	0.22
Anxiety disorder	0.23	-0.82; 1.29	0.66	0.09	-1.30; 1.49	0.89	-0.44	-2.02; 1.14	0.58
Positive arguments for FSD	0.05	-1.15; 1.26	0.50	0.65	-0.96; 2.27	0.50	-0.87	-2.65; 0.91	0.33
Clinical or paraclinical explanation	2.11	0.06; 4.17	0.04	2.16	-0.57; 4.88	0.45	2.73	-2.18; -7.64	0.27
Physical activity recommendation									
No rehabilitation	0.93	-1.90; 3.76	0.52	1.50	-2.23; 5.23	0.43	2.87	-2.44; 8.17	0.29
Self-rehabilitation with exercise program	-0.22	-2.57; 2.13	0.85	1.40	-1.70; 4.49	0.37	1.19	-3.59; 5.96	0.62
Rehabilitation in ambulatory structure	-0.74	-3.14; 1.66	0.54	0.65	-2.53; 3.82	0.69	1.44	-3.32; 6.19	0.55
Hospital rehabilitation program	2.11	-2.66; 2.16	0.83	2.11	-1.07; 5.29	0.19	0.99	-3.89; 5.88	0.69
SF-36 physical component score	-	-	-	-	-	-	-0.05	-0.10; 0.01	0.09

B: unstandardized beta regression coefficient; CI: Confidence Interval; SF-36: 36-item Short-Form Health survey questionnaire.

be both clinically inaccurate and perceived as stigmatizing. Nevertheless, in line with the literature [14,44,45], depression and anxiety were frequent in our population and may have contributed to some extent to some persistent symptoms such as fatigue and cognitive dysfunction for depression or palpitations and shortness of breath for anxiety [46,47].

The lack of abnormal clinical findings or test results in most of our patients is consistent with the clinical practice-based literature on post-COVID-19 symptoms, where a striking contrast between the severity of symptoms and the normality of physical examination and extensive routine laboratory tests is frequently reported [9,10,48]. This also might be due to subtle or still unknown pathophysiological features. Indeed, several pathophysiological hypotheses have been proposed to account for the persistence of symptoms after COVID-19 (e.g., micro-clots, abnormalities of microbiome, exhausted T-cells, viral persistence). However, to the best of our knowledge, none of these hypotheses translate into clinically interpretable tests to date, due to a large overlap between patients previously infected with SARS-CoV-2 with and without long COVID. In this context, available clinical practice guidelines do not recommend these tests while stressing the drawbacks of excessive testing such as increased risk for incidental findings, anxiety about abnormal results that do not have clinical significance, or imaging-related radiation exposure [5].

The cognitive and behavioral mechanisms that are thought to underlie functional somatic disorders may contribute to explain this clinical feature [39,49]. Psychological factors may influence the perception of symptoms through increased attention or biased expectation [25,26]. The belief that physical activity should be avoided until full recovery may lead to hypervigilance and physical deconditioning [50]. Physical deconditioning was frequent in our population, with 91.2% of patients who were given recommendation regarding physical rehabilitation of impaired standardized physical tests performed by the adapted physical activity specialists. Among them, 22.6% of all patients who were recommended a hospital rehabilitation program, because their chance to recover either at home with a personalized program or with the help of a specific certified sport center was deemed very low by the adapted physical activity specialists.

Validated treatments for persistent symptoms after COVID-19 are still lacking. The diagnosis of functional somatic disorder suggests that some treatment options such as cognitive behavioral therapy [51] could be promising, without excluding other treatments. Supervised physical activity and cognitive behavioral therapy are validated treatments for functional somatic disorders such as chronic fatigue [52] or fibromyalgia [53].

Clinicians may fear that the diagnosis of functional somatic disorder could be perceived as stigmatizing by patients [54]. This assumption was not supported by our results, given the high levels of satisfaction of patients observed overall, including those who were diagnosed with a functional somatic disorder. Of note, being a woman was associated with lower levels of satisfaction. This result warrants further examination but it is noteworthy that it did not depend upon the medical conclusions and that levels of satisfaction remained high in both men and women. This high level of satisfaction might result from our approach that does not oppose psychological mechanisms to other mechanisms [24]. Indeed, although the conclusion of clinical or paraclinical abnormal findings potentially explaining the symptoms was associated with higher levels of overall satisfaction, the conclusion of positive arguments in favor of a diagnosis of functional somatic disorder did not alter satisfaction levels. It might result from specific characteristics of the program including the comprehensive medical workup and the brief psychoeducational intervention delivered during the psychiatric consultation. Most patients welcomed these explanations as opposed to labels they were previously facing such as “medically unexplained symptoms” or stigmatizing statement such as “it’s all in your head”. Whether this psychoeducational intervention and the subsequent proposed care may improve persistent physical symptoms will be the focus of further studies.

This study has some strengths. First, we included a relatively large clinical sample of consecutive patients. Second, we provided these patients with a systematic multidisciplinary assessment, including laboratory tests according to a guideline-based algorithm, a comprehensive clinical assessment, and an extensive evaluation of physical, mental and functional dimensions with validated tools. Third, we systematically assess the presence of positive arguments for a diagnosis of functional disorder, related to potential mechanisms, and not only negative arguments based on the lack of abnormal findings from physical examination or routine tests, which may miss subtle or yet unknown anomalies. This study has also some limitations. First, our results were obtained in a population of patients attending a tertiary care structure, thus limiting their generalizability. For instance, this recruitment bias might have increased the severity of the persistent symptoms or the proportion of clinical pictures consistent with a diagnosis of functional somatic disorder. Second, psychiatric diagnoses were all made by a trained clinician (CG, COV, VP, CL) on the basis of the DSM-5 criteria but without using a structured interview. Third, only half of the patients responded to the satisfaction survey, which could have induced a selection bias regarding satisfaction results.

5. Conclusion

In this tertiary multidisciplinary day-hospital program dedicated to the evaluation of symptoms persistent for >2 months after a documented or self-reported infection with SARS-CoV-2, a high proportion of patients presented with both positive and negative arguments for a diagnosis of functional somatic disorder. Such a diagnosis was generally well accepted by the patients, as shown by the high levels of satisfaction, and was an opportunity to offer them appropriate care. Further research on the mechanisms of long COVID should therefore explore cognitive and behavioral mechanisms that may lead to functional somatic disorder as well as the potential efficacy of cognitive and behavior therapy or progressive physical rehabilitation in this context.

Contributors

C. Gouraud, B. Ranque, C. Lemogne and P. Thoreux designed the study; C. Gouraud, B. Ranque, C. Lemogne, C. Ouazana-Vedrine and V. Pitron worked on literature search; S. Betouche, S. Guemouni, C. Gouraud and Kewei Xiang contributed to collection and assembly of data; C. Gouraud, C. Lemogne, B. Ranque, E. Caumes contributed to data analysis and interpretation; C. Ouazana-Vedrine, V. Pitron, K. Bolloch and E. Caumes provided technical support. All authors have contributed to interpretation and critically reviewed the manuscript. All authors approved the final version of the manuscript.

Ethics approval

This study has obtained the authorization from the “Comité d’éthique de la recherche AP-HP Centre” (CERAPHP); IRB registration #00011928, Ref 2022–10-08.

Data statement

The data underlying the findings of our study are not publicly available due to legal reasons related to data privacy protection in the context of usual care.

Study group

The CASPer-COVID Study Group includes eleven, infectious diseases specialists (M. Belan, D. Batisse, E. Canoui, E. Caumes, M. Karmochkine, P. Parize, A. Pouvaret, J. Pavie, A. Serris, L. Slama, J-P. Viard), twelve internists (J-B. Arlet, G. Cheminet, E. Flammarion, P. Getten, E. Lafont, C. Manoli, A. Michon, B. Ranque, N. Senot, O. Steichen, J. Tennebaum,

A. Vanjak), one general physician (K. Xiang), four adapted activity specialists (K. Bolloch, V. Goyat, E. Lerondeau, C. Verot), one sports medicine physician (P. Thoreux) and five psychiatrists (C. Gouraud, C. Lemogne, C. Ouazana-Vedrines, L. Rotenberg, V. Pitron).

Declaration of Competing Interest

The authors have no competing interests to report.

Acknowledgements

CL and BR are supported by two grants “AAP Covid long 2022-1” from the Agence nationale de recherche sur le sida | Maladies infectieuses émergentes. CL and CG are supported by a grant from “la Fondation de l’AP-HP (Assistance Publique - Hôpitaux de Paris)”.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jpsychores.2023.111475>.

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