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RESEARCH ARTICLE

The Role of Illness Severity and Emotional Distress in General and Cognitive Rehabilitation of Individuals with Post-COVID-19

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Abstract

Background and aims: Emotional distress is widespread among individuals recovering from COVID-19. The present study examined the relationships between illness severity and emotional distress and the outcomes of a general and cognitive rehabilitation program.

Methods: Participants were 61 post-acute COVID-19 patients who participated in a multidisciplinary rehabilitation program. Data were collected at admission and discharge, 6 months later. Medical evaluations and self-reported emotional, neuropsychological and functional measures were used.

Results: Mild illness was associated with higher levels of self-reported anxiety and depression and with lower self-reported executive functioning. Elevated anxiety levels and lower cognitive profile at admission were significantly linked to poorer cognitive outcomes, but not to motor or general functioning level at discharge.

Conclusions: The results of the study indicate the significance of monitoring emotional characteristics, particularly anxiety, in post-COVID-19 individuals during multidisciplinary rehabilitation.

Keywords: COVID-19, emotional distress, multi-disciplinary rehabilitation, cognitive functioning, executive functioning

Introduction

COVID-19 is associated with significant emotional distress. In October 2021, Groff et al.¹, published a meta-analysis that systematically evaluated post-acute sequelae of COVID-19 based on 57 studies. Anxiety disorders (29.6%) and difficulties in concentrating (23.8%) were among the most prevalent symptoms. High levels of moderate-to-severe anxiety (14%) and depression (19%) were reported also in a UK study of post-COVID-19 patients². In Italy, post-COVID-19 patients reported significant levels of anxiety (42%), posttraumatic stress disorder (PTSD, 28%), depression (31%), obsessive-compulsive symptoms (20%), and insomnia (40%)³.

Studies have investigated the effect of emotional distress and cognitive characteristics on rehabilitation outcomes in other diseases^{4, 5}, but only limited data exist about the influence of these parameters in post-COVID-19 rehabilitation. Poor rehabilitation outcomes were reported in patients with sustained psychological disorder after traumatic brain injury (TBI)⁶ and stroke^{7, 8}. Similarly, lower scores on MoCA have been associated with reduced gain on the Functional Independence Measure (FIM) in post-stroke patients^{9, 10}. In post-COVID-19 patients, however, data about the connections of these factors with rehabilitation outcomes is limited and usually only short-term data on follow-ups are available^{11, 12}.

The present study examined the associations between illness severity, its consequent emotional distress and cognitive characteristics, and the outcomes of a multidisciplinary rehabilitation program in post-COVID-19 patients. The results may contribute to developing psychological and cognitive interventions to improve the outcomes of rehabilitation for post-COVID-19 patients.

Methods

Participants

We recruited 61 post-acute COVID-19 patients out of 65 patients who were referred to the rehabilitation program at Hadassah University Hospital in Jerusalem due to COVID-19 between December 2020 and August 2021. The multidisciplinary rehabilitation program included respiratory and endurance physical therapy, cognitive therapy, individual psychological treatment, and a social support group. Twenty-five of the severe patients were admitted to inpatient rehabilitation directly from the acute hospitalization in a COVID-19 ward, after which they joined an outpatient post-COVID-19 customized rehabilitation program. The remaining 36 patients were admitted directly to the outpatient program. Participants who matched the inclusion criteria and

agreed to participate in the study were prospectively enrolled and signed an informed consent form. Inclusion criteria were: age 18 years or older, PCR confirmed COVID-19 infection in the previous year, Mini-Mental State Examination (MMSE) score above 24 (according to IRB request), and able to understand and sign an informed consent form. Exclusion criteria were: pre-morbidity of mental disorder or dementia and post-COVID-19 cerebrovascular accident with severe cognitive impairment. 4 patients were excluded from the study due to these criteria. Ethical approval was granted by the Hadassah Medical Center IRB committee (number 0943-20-HMO).

Tools and Protocol

Data were collected at admission to the rehabilitation program, and at discharge 3.7+₋2.3 months after acute illness, and 7.2+₋3.2 months, respectively. The data included hospital records, functional measures, and self-report questionnaires. All questionnaires were given in a translated validated version (Hebrew or Arabic).

Demographic, Clinical, and Functional data

Demographic data were extracted from hospital records. They included age, gender, duration of acute hospitalization, duration of ventilation, and duration of rehabilitation.

World Health Organization (WHO) clinical progression scale (CPS). Illness severity was measured by the WHO-CPS. The scale ranges from 0 (uninfected) to 10 (dead), and values 1-9 are divided into groups of ambulatory mild disease, hospitalized moderate disease, and hospitalized severe disease¹³.

Functional Independence Measure (FIM). FIM is one of the most widely used measures of assessing the basic quality of daily living activities in individuals with a disability¹⁴. It is comprised of 18 items grouped into motor and cognition subscales. Each item is scored on a scale ranging from 1 (total assistance or not testable) to 7 (performs independently in a safe and timely manner). Higher scores reflect greater independence in activities of daily living¹⁵. This measure was assessed prospectively, at admission to and at discharge from the rehabilitation program.

Emotional distress

Hospital Anxiety and Depression Scale (HADS). Anxiety and depression were measured by HADS, a self-report scale containing 14 statements divided into two subscales measuring symptoms of depression and anxiety¹⁶. Responses are provided on a four-point scale ranging from 0 to 3, a higher score indicating a worse condition. The maximum

total score for each subscale is 21. Several studies suggest a cut-off score of ≥ 8 as optimal for best sensitivity and specificity^{17 18}.

Impact of Event Scale - Revised (IES-R). We assessed post-traumatic symptoms by the IES-R, a self-report scale containing 22 items that assesses current psychological distress symptoms due to a particular stressful event¹⁹. In the present study, participants were asked to answer the IES-R in relation to the COVID-19 pandemic. Participants were asked to rate on a 5-point Likert scale how distressing each difficulty described by the items has been for them, ranging from 0 (not at all) to 4 (extremely). A higher score indicates greater distress. A score of 33 was considered the cut-off point²⁰.

Posttraumatic Growth Inventory (PTGI). We measured posttraumatic growth by the PTGI, a self-report scale containing 21 items that measure positive outcomes reported by people who have experienced traumatic events²¹. Participants were asked to rate the degree to which they experienced the changes described by each item on a 6-point Likert scale ranging from 0 ("I didn't experience this change as a result of my crisis") to 5 ("I experienced this change to a very great degree as a result of my crisis"). A higher score indicates a higher level of posttraumatic growth.

Fatigue Severity Scale (FSS). We measured fatigue level by the FSS, a self-report scale containing 9 items that assess fatigue as a symptom of a variety of chronic conditions and disorders²². The scale addresses the effects of fatigue on daily functioning and its connection to motivation, physical activity, work, family, and social life. Participants were asked to rate the ease with which they became fatigued and the degree to which the symptom posed a problem for them on a 7-point Likert scale ranging from 1 (completely disagree) to 7 (completely agree). A lower score indicates less fatigue. The recommended cut-off for the healthy population is 2.3²³.

Visual Analogue Scale (VAS). We measured pain by the VAS²⁴. Each participant marked the perceived level of pain on a scale of 0 (no pain) to 10 (worst imaginable pain).

Cognitive functioning

Montreal Cognitive Assessment (MoCA). The MoCA is a 30-point screening tool that assesses multiple cognitive domains. The suggested cut-off for normal functioning in the Israeli population is 26 points out of 30, with correction for age and education²⁵.

Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A). We assessed executive functions with BRIEF-A²⁶, a self-report scale containing 75 standardized items that measure

various aspects of executive functions on 9 subscales: Inhibition, Shifting, Emotional control, Self-monitoring, Initiation, Working memory, Planning, Organization of material, and Task monitoring. The 9 subscales combine to form the Behavior Regulation Index (BRI), the Metacognition Index (MI), and a composite summary score (Global Executive Composite, GEC). For each scale, T scores can be derived, with higher scores reflecting a greater degree of executive dysfunction and level of impairment, and scores at or above 65 suggestive of clinical significance.

Statistical analysis

Data were entered into a Microsoft Excel file (Microsoft, Redmond, WA, USA), then transferred to a statistical analysis program (SPSS 26.0, Chicago, IL, USA). We used Pearson's correlations to examine the relations between all variables, and linear regression analysis to examine which variables predicted the cognitive function at discharge from rehabilitation, as measured by cognitive FIM. $P < 0.05$ was considered to be significant.

Results

A. Demographic and emotional and cognitive characteristics among 61 patients at admission to the rehabilitation program

The demographic, emotional and cognitive characteristics of the 61 post-COVID-19 participants, at admission to the rehabilitation program are presented in Table 1. Average age was 54.1 (SD=15.3) and 39.3% were older than 60; 34% (n=21) were female. The average duration of the rehabilitation program was 3.2 ± 2.1 months. The mean \pm SD of their WHO-CPS was 6.3 ± 2.4 (range 2-9). Meaningful levels (cut-off=8) of anxiety and depression were detected in 52% (n=37) and 59% (n=29) participants, respectively, as revealed by the HADS questionnaire. A significant level (cut-off=33) of posttraumatic symptoms was reported by 73% (n=38) of the sample, as measured by the IES-R. The mean \pm SD of posttraumatic growth, as reported in the PTGI, was 58.9 ± 25.2 . Significant fatigue level (cut-off=2.3) was reported by all participants. The mean perceived level of pain was 3.6 (SD=3.3), as measured by the VAS. The mean MoCA was 23.6 (SD=3.7). A significant decrease, compared to the norms in a sample of healthy and sick people in Israel (Roth et al., 2005), was noted in most of the BRIEF-A scales. All participants showed valid BRIEF-A profiles. Fifty-two percent (n=37) were above the abnormal threshold ($T \geq 65$) on the GEC index, indicating lower self-reported executive functioning as compared to another sample of healthy and sick people in Israel.

Table 1. Demographics, emotional and cognitive characteristics of 61 patients during the acute illness

Variable		Average / n	Range / %
Age	Average age, years	54.1 ± 15.3	18 to 84
	Above 60 years	N=24	39.3%
Gender, female		N= 21	34%
Race, jews		N=44	72%
Average WHO-CPS		6.3 ± 2.4	2 to 9
Average duration of acute hospitalization (weeks)		5.5 ± 4.2	0 to 16
Average duration of ventilation (days)		17.4 ± 19.6	0 to 90
Average duration of rehabilitation (months)		3.2 ± 2.1	1 to 12
Average HADS - Anxiety		8.6 ±6.5	0 to 29
Average HADS - Depression		9.1 ±5.6	0 to 29
Average IES-R		43.8 ±21.7	0 to 77
Average PTGI		58.9 ±25.2	0 to 101
Average FSS		5.6 ± 1.1	2.4 to 7
Average VAS		3.6 ± 3.3	0 to 10
Average MoCA		23.6 ± 3.7	14 to 30
MoCA < 26		N=36	62%
BRIEF-A: Global Executive Composite (N of T ≥65)		N=37	52%

Note: WHO-CPS= World Health Organization clinical progression scale; MoCA=The Montreal Cognitive Assessment; HADS=Hospital Anxiety and Depression Scale; IES-R=Impact of Event Scale - Revised; PTGI=Posttraumatic Growth Inventory; FSS=Fatigue Severity Scale; VAS=Visual Analogue Scale; BRIEF-A=Behavior Rating Inventory of Executive Function-Adult Version.

B. Correlations between disease severity, emotional and cognitive characteristics at admission to rehabilitation

The correlations between disease severity, emotional distress and cognitive characteristics measured at admission to rehabilitation are presented in Table 2. Disease severity was negatively correlated with anxiety, depression, and global executive functioning. Fatigue was negatively correlated only with WHO-CPS,

and pain level based on the VAS was negatively correlated only with days of ventilation. Disease severity indices, including WHO-CPS, weeks of hospitalization in ICU, and days of ventilation were negatively correlated with motor and total FIM at admission. We found no significant correlations between cognitive FIM, MoCA results, posttraumatic symptoms measured by IESR and PTGI, and the parameters of acute COVID-19 infection.

Table 2. Pearson's correlations coefficient between disease severity, emotional and cognitive characteristics at admission to rehabilitation

	Ventilation days	WHO-CPS	Cognitive-FIM - admission	Motor-FIM - admission	Total - FIM - admission	MoCA	HADS Anxiety	HADS Depression	IESR	PTGI	FSS	Brief-GEC	VAS
Weeks of acute hospitalization	0.827*	0.807*	-0.124	0.669*	0.676*	0.038	0.415*	0.310*	-0.093	0.167	-0.154	0.282*	0.185
Ventilation days		0.670*	0.115	0.466*	0.442*	0.099	0.352*	0.318*	-0.086	0.056	-0.035	0.297*	0.269*
WHO-CPS			0.056	0.471*	0.455*	-0.064	0.562*	-.507**	-0.220	0.225	0.332*	0.376**	0.106
Cognitive-FIM - admission				0.042	0.188	0.260*	-0.059	-0.037	-0.035	-0.098	-0.048	0.225	-0.096
Motor-FIM - admission					0.989*	-0.142	0.336*	0.177	0.081	-0.175	-0.020	0.174	0.125
Total-FIM - admission						-0.101	0.319*	0.167	0.073	-0.186	-0.027	0.136	0.109

Note: WHO-CPS=World Health Organization Clinical Progression scale; FIM=Functional Independence Measure; MoCA=The Montreal Cognitive Assessment; HADS=Hospital Anxiety and Depression Scale; IES-R =Impact of Event Scale - Revised; PTGI=Posttraumatic Growth Inventory; FSS=Fatigue Severity Scale; BRIEF-A=Behavior rating inventory of Executive Function-Adult Version; VAS=Visual Analogue Scale.

* Correlation is significant at the 0.05 level (2-tailed),

** Correlation is significant at the 0.01 level (2-tailed).

C. Correlations between emotional and cognitive characteristics at admission and functional level at discharge from rehabilitation

Correlations between emotional and cognitive characteristics at admission and functional level at discharge measured by total, motor, and cognitive FIM at discharge from rehabilitation are presented in Table 3.

Anxiety was negatively correlated with cognitive FIM at discharge. Pain correlated positively only with motor function at discharge. No other

significant correlations were found between depression, PTSD measured by IESR, PTGI, and fatigue and functional level at discharge.

Impaired cognitive and executive functions at admission, as measured by the MoCA and BRIEF-A, were correlated with lower cognitive function at discharge (cognitive FIM). Yet, we found no significant correlations between these measurements, taken at admission, and functional level at discharge.

Table 3: Pearson's correlations coefficient between emotional and cognitive characteristics at admission and functional level at discharge

	Cognitive -FIM - admission	Motor-FIM - admission	Total -FIM -admission	MoCA	HADS Anxiety	HADS Depression	IESR	PTGI	FSS	BRIEF-GEC	VAS
Cognitive-FIM - discharge	0.48**	-0.36**	-0.28*	0.435*	-0.400**	-0.243	-0.269	-0.042	-0.067	0.430**	-0.202
Motor-FIM - discharge	-0.11	0.52**	0.5**	0.127	0.148	0.051	0.135	-0.089	0.184	0.065	0.271*
Total -FIM - discharge	-0.01	0.46**	0.45**	0.221	0.065	0.000	0.080	-0.099	0.172	-0.026	0.234

Note: FIM=Functional Independence Measure; MoCA=The Montreal Cognitive Assessment; HADS=Hospital Anxiety and Depression Scale; IES-R=Impact of Event Scale - Revised; PTGI=Posttraumatic Growth Inventory; FSS=Fatigue Severity Scale; BRIEF-A=Behavior Rating Inventory of Executive Function-Adult Version; VAS=Visual Analogue Scale.

* Correlation is significant at the 0.05 level (2-tailed),

** Correlation is significant at the 0.01 level (2-tailed).

D. Emotional and cognitive characteristics as predictors of functioning at discharge: A regression analysis.

We performed a blockwise linear regression analysis to predict which of the emotional and cognitive parameters contribute significantly to total, motor, and cognitive FIM at discharge (Table

4). The model was significant only in explaining 39% of the variance in cognitive FIM at a level of 0.00. MoCA and HADS anxiety contributed significantly to the model. The model was insignificant in explaining the variables predicting total and motor FIM (data not shown).

Table 4: Linear regression to predict cognitive FIM at discharge

Model	Unstandardized coefficients		Standardized coefficients	t	Sig.
	B	Std. Error	Beta		
MoCA	0.165	0.053	0.397	3.104	0.003
HADS Anxiety	-0.126	0.056	-0.554	-2.264	0.029
HADS Depression	0.086	0.053	0.328	1.638	0.109
IESR	0.007	0.012	0.097	0.553	0.583
FSS	0.106	0.176	0.081	0.603	0.549
VAS	-0.062	0.057	-0.132	-1.086	0.283
BRIEF-GEC	-0.014	0.014	-0.171	-0.962	0.341

Note: FIM=Functional Independence Measure; MoCA=The Montreal Cognitive Assessment; HADS=Hospital Anxiety and Depression Scale; IES-R=Impact of Event Scale - Revised; FSS=Fatigue Severity Scale; VAS=Visual Analogue Scale; BRIEF-A-GEC= Behavior Rating Inventory of Executive Function-Adult Version, Global Executive

Discussion

This study examined the associations between the severity of acute COVID-19 illness, its consequent emotional and cognitive characteristics, and the outcomes of rehabilitation program. We found that participants at admission to the rehabilitation program reported high levels of emotional distress, including anxiety, depression, posttraumatic symptoms, and fatigue. This finding is consistent with previous studies indicating a high incidence of depression and anxiety symptoms in individuals with long-term complications after critical care and chronic diseases^{27 28 29 30}, specifically following COVID-19 infection³¹.

Yet, contrary to our initial expectation, the findings indicated that greater illness severity was

associated with less anxiety, less depression, and better executive functioning, while lower levels of disease severity were correlated with increased symptomatology. A possible explanation of this finding may be found in theories of coping strategies³². Individuals with severe illness tend to use active strategies (problem-focused coping) or protective mechanisms (e.g., denial). By contrast, patients whose illness is less severe typically use emotion-focused strategies, therefore their levels of anxiety, depression, and fatigue are elevated³³. Although there are abundant reports in the literature of severe illness associated with greater anxiety, in one study of cardiac patients no correlation was found between the severity of cardiac illness and the level of anxiety³⁴.

Furthermore, similarly to our findings, in several longitudinal studies of patients with multiple sclerosis, lower levels of disease severity at early stages were correlated with higher levels of anxiety^{35 36}.

Participants who were classified as having severe acute illness reported that they performed better on executive functions than those who were classified as less severe acute illness. This may be because these patients had been more affected by basic motor and functional deficiencies, and were possibly less attentive to higher functions such as planning and monitoring. Similar finding has been found in other populations, such as in Parkinson's disease, where patients with executive deficits were unable to recognize their limitations while performing tasks³⁷. Alternatively, patients may have reported that their executive functioning remained intact despite their severe illness because of a lack of awareness of the impairments, which may also explain their self-reported better emotional status. In this study, we relied on self-report questionnaires and not on observations of family members, therefore reports may have been biased. Similarly, in a study conducted on patients with traumatic brain injury, no correlation was found between objective and subjective reports on executive functions, but a correlation was found between subjective reporting and emotional distress³⁸.

A main objective of this study was to evaluate the relationship of the emotional and cognitive profiles at admission with rehabilitation outcomes. We found that high levels of anxiety at admission were negatively correlated with cognitive functioning at discharge. This finding is consistent with previous studies, indicating that high anxiety levels are negatively associated with cognitive performance^{3940 41}. Another factor that affected cognitive level at discharge was, as expected, lower cognitive status at admission (as measured by MoCA, cognitive FIM, and BRIEF-A).

At the same time, initial cognitive and emotional status did not affect motor and total functioning at discharge. In contrast to our findings, studies on post-stroke patients found that cognitive impairment was associated with lower rehabilitation improvements^{42 10}. This difference may be explained by the profound influence of cognitive function on stroke patients as opposed to its lower influence on the rehabilitation of COVID-19 patients.

Although already described a high level of anxiety and depression in COVID-19 patients^{43 44}, the correlation between these emotional parameters and functional outcomes of rehabilitation was not described previously. In the

present study, neither anxiety nor depression was correlated with motor or total FIM at discharge. In other diseases, anxiety and depression had a deleterious effect on rehabilitation outcomes^{7 8}. For example, in a study of 950 patients after traumatic brain injury, of whom 46% presented with moderate-to-severe anxiety at admission, those with moderate and severe anxiety experienced higher levels of disability and demonstrated poorer functional performance than did the groups with mild anxiety or none⁴⁵. A study on post-stroke patients, of whom 57% were diagnosed with depression, found a significant correlation between the level of depression and functional disability⁴⁶. A possible explanation of the difference between our results and those in other diseases may have to do with the finding that in the present study patients with severe illness reported less emotional distress despite their lower level of functioning at the beginning of the rehabilitation period.

In this study, neither posttraumatic stress signs nor posttraumatic growth was found to be associated with functional outcomes or any other variable. Studies indicated a high PTSD rate in COVID-19 patients⁴⁷, whereas posttraumatic growth was described only in a few studies, mainly of healthcare workers^{48 49}. A possible explanation is that because the COVID-19 crisis was still ongoing at the time of the study, it was too early to develop signs of posttraumatic growth, which typically develops gradually following the cessation of the traumatic event⁵⁰.

The present study has several limitations. First, it comprises a relatively small number of participants, most of whom men, however we included almost every COVID-19 patient who agreed to participate in the study. Secondly, self report measures were used, which reflect the subjective experience of the patients rather than objective measures. Finally, there was no control group who did not get rehabilitation treatment; however, taking into account the WHO recommendation of rehabilitation for COVID-19 patients we considered it unethical to have a group without rehabilitation treatment.

Conclusion

This study showed that COVID-19 patients reported high levels of emotional distress including anxiety, depression, and other posttraumatic symptoms at admission to rehabilitation, but the severity of these symptoms was negatively associated with the severity of the acute COVID-19 infection. We found that higher anxiety levels and lower cognitive scores at admission were significantly linked with poor cognitive rehabilitation outcomes, but not with motor and

general functional level at rehabilitation discharge. The results highlight the importance of monitoring and treating the emotional characteristics of COVID-19 patients, particularly anxiety, because these factors may affect their cognitive abilities during multidisciplinary rehabilitation.

Notes

Conflict of Interest: The authors have no conflicts of interest to declare.

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Ethics Statements: Ethical approval was granted by the Hadassah Medical Center IRB committee (number 0943-20-HMO).

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