

## Post-COVID Quality of Life and Functional Status in Patients with and Without Diabetes Mellitus

### Qualidade de Vida e Status Funcional Pós-COVID em Pacientes com e sem Diabetes Mellitus

Rachel Bastos Nazareno dos Anjos<sup>a</sup>; Fernanda Rodrigues Fonseca<sup>b</sup>; Flávia Del Castanhel<sup>b</sup>; Rosemeri Maurici<sup>a,c</sup>

<sup>a</sup>Universidade Federal de Santa Catarina, Programa de Pós-Graduação em Ciências Médicas. SC, Brazil.

<sup>b</sup>Universidade Federal de Santa Catarina. SC, Brazil.

<sup>c</sup>Hospital Universitário Professor Polydoro Ernani de São Thiago. SC, Brazil.

E-mail: [rachel.bastos8@gmail.com](mailto:rachel.bastos8@gmail.com)

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#### Abstract

Endocrine manifestations in post-acute COVID-19 may result from direct viral lesions or immunological and inflammatory causes. COVID-19 may exacerbate the pre-existing inflammatory state in diabetes mellitus. This study aimed to describe the functional status and quality of life of adults and older people after hospitalization for COVID-19, comparing diabetics and non-diabetics. This observational study evaluated patients with or without diabetes/pre-diabetes at 73 (n=53) and 376 (n=52) days of convalescence from COVID-19. In functional status, respectively in assessments 1 and 2, the score on the Post-COVID-19 Functional Status scale (PCFS) was 2 (1–3) and 2 (0–2), being 75.5% and 72.5% the frequency of participants with very mild, mild, moderate, or severe functional limitations. In quality of life, the frequencies of participants with mild, moderate, severe, or extreme problems in the EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) domains were 39.6% in mobility, 17.0% in self-care, 45.3% in usual activities, 73.6% in pain/discomfort, and 71.7% in anxiety/depression in the first assessment; 34.6% in mobility, 9.6% in self-care, 37.3% in usual activities, 73.1% in pain/discomfort, and 65.4% in anxiety/depression in the second assessment. The EQ-5D-5L Visual Analogue Scale (VAS) score was 70 (50-90) in Assessment 1 and 80 (60-90) in Assessment 2. There were no differences in PCFS and EQ-5D-5L scores nor associations with their items between diabetic and non-diabetic groups. Diabetes mellitus, therefore, does not seem to influence quality of life and functional status in the first year after hospitalization for COVID-19.

**Keywords:** Diabetes Mellitus. COVID-19. Quality of Life.

#### Resumo

Manifestações endócrinas na COVID-19 pós-aguda podem decorrer de lesões virais diretas ou causas imunológicas e inflamatórias. A COVID-19 pode exacerbar o estado inflamatório preexistente no diabetes mellitus. O objetivo deste estudo foi descrever estado funcional e qualidade de vida de adultos e idosos após hospitalização por COVID-19, comparando diabéticos e não-diabéticos. Foi um estudo observacional que avaliou pacientes com ou sem diabetes/pré-diabetes aos 73 (n=53) e 376 (n=52) dias de convalescença da COVID-19. No estado funcional, respectivamente nas avaliações 1 e 2, o escore na Post-COVID-19 Functional Status scale (PCFS) foi 2 (1–3) e 2 (0–2), sendo 75,5% e 72,5% a frequência de participantes com limitações funcionais muito leves, leves, moderadas ou graves. Na qualidade de vida, as frequências de participantes com problemas leves, moderados, graves ou extremos nos domínios do EuroQol 5 Dimensions 5 Levels (EQ-5D-5L) foram 39,6% em mobilidade, 17,0% em autocuidado, 45,3% em atividades habituais, 73,6% em dor/desconforto e 71,7% em ansiedade/depressão na primeira avaliação; 34,6% em mobilidade, 9,6% em autocuidado, 37,3% em atividades habituais, 73,1% em dor/desconforto e 65,4% em ansiedade/depressão na segunda avaliação. O escore da Escala Visual Analógica (VAS) do EQ-5D-5L foi 70 (50-90) na Avaliação 1 e 80 (60-90) na Avaliação 2. Não houve diferenças nos escores e nem associações com os itens da PCFS e do EQ-5D-5L entre os grupos diabéticos e não-diabéticos. O diabetes mellitus, então, parece não influenciar a qualidade de vida e o estado funcional no primeiro ano após hospitalização por COVID-19.

**Palavras-chave:** Diabetes Mellitus. COVID-19. Qualidade de Vida.

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## 1 Introduction

Post-COVID-19 syndrome (PCS) has been defined as the persistence of signs and symptoms for more than 12 weeks after acute Coronavirus disease (COVID-19) infection, which are not explained by an alternative diagnosis.<sup>1</sup> The most prevalently reported symptoms in PCS are fatigue, sleep disturbance, dyspnea, ageusia, anosmia, chest pain, headache, and cough.<sup>2</sup> This syndrome has a significant incidence, as shown in an Italian study including 143 patients discharged from the hospital after recovery from COVID-19, in which only 18 patients (12.6%) did not show any symptoms after a

period of approximately 60 days since the onset of symptoms.<sup>3</sup>

There are some predictive factors that contribute to the occurrence of PCS. The risk of PCS is more likely in patients with more than 5 symptoms during the acute phase of COVID-19 and in patients who are elderly, obese, and diabetic.<sup>4,5</sup> Carvalho-Schneider et al. reported that hospitalization during acute infection and age between 40 and 60 years were considered the most significant predictors for the development of PCS.<sup>6</sup>

A significant number of patients do not recover 6 months after hospital discharge, as shown in a prospective multicenter

study, in which only 20% to 30% recovered completely, and the non-recovery of most patients during this period was associated with the female sex, middle age (40 to 59 years), the presence of 2 or more comorbidities, and mechanical ventilation.<sup>7</sup>

Symptoms may persist for at least 1 year in a considerable proportion of COVID-19 survivors, and they are more evident in women and patients with more severe acute COVID-19 infection, as demonstrated by a systematic review and meta-analysis.<sup>8</sup>

The number of symptoms during the initial phase of the disease seems to influence the occurrence of PCS. The quantity of symptoms present in the initial phase of COVID-19 infection contributes to patients experiencing persistent fatigue.<sup>9</sup>

Göertz et al.<sup>10</sup> showed the presence of multiple symptoms 3 months after infection, in both hospitalized and non-hospitalized patients. Another study that evaluated patients 2 months after severe COVID-19 infection showed that there was no association between the presence or absence of preexisting comorbidities and the persistence of symptoms such as fatigue, sleep disturbance, and pain.<sup>11</sup>

One of the most common complaints observed in PCS is fatigue.<sup>12</sup> Fatigue or muscle weakness and sleep disturbances are the most common symptoms 6 months after hospitalization due to COVID-19.<sup>13</sup> Nonetheless, the symptom of fatigue varies among patients, and preexisting diagnosis of depression is associated with severe post-COVID-19 fatigue.<sup>12</sup>

The association between long COVID and different variants of the SARS-CoV-2 virus remains uncertain; however, a study showed that the prevalence of long COVID among healthcare professionals could vary between pandemic waves, from 48.1% during the first wave (February to September 2020 [wild-type variant]), to 35.9% during the second wave (October 2020 to July 2021 [alpha variant]), and 16.5% during the third wave (August 2021 to March 2022 [delta and omicron variants]).<sup>14</sup> Further studies are needed to investigate the risks of PCS according to the different variants of SARS-CoV-2.

The estimated global prevalence of PCS is 43%, and patients who were hospitalized during acute COVID-19 infection had a higher prevalence of PCS (54%), compared to non-hospitalized patients (34%).<sup>15</sup>

Type 2 diabetes mellitus has a bidirectional relationship with COVID-19.<sup>16</sup> Poorly controlled diabetes increases the severity of COVID-19 and is associated with increased mortality and morbidity,<sup>17</sup> and COVID-19 has also been observed to result in worse glycemic control, progression from pre-diabetes to diabetes, increased number of symptoms, and increased corticoid-induced diabetes.<sup>18</sup>

Comorbidities, such as diabetes, hypertension, and cardiovascular disease, are risk factors for the severity and mortality of people infected with COVID-19.<sup>19</sup>

Although some studies have shown the expression of = Angiotensin Converting Enzyme-2 (ACE2) and type II transmembrane serine protease (protease involved in the entry of SARS-CoV-2 into the cell) in  $\beta$  cells,<sup>20</sup> the primary deficit in insulin production is probably mediated by factors such as the inflammatory state of the disease or the stress response due to infection and peripheral insulin resistance.<sup>21</sup>

There is evidence that patients with diabetes have higher levels of inflammatory markers, increased risk of severe pneumonia, more intense inflammatory response, higher levels of D-dimer and fibrinogen, and hypercoagulability compared to patients without diabetes.<sup>22</sup>

Patients with diabetes are more prone to thrombotic events, and data have shown that thrombotic events are a frequent complication during COVID-19 infection.<sup>23</sup> Type 2 diabetes mellitus can cause microvascular complications, involving the eyes, nerves, and kidneys; however, we do not know whether these complications may be exacerbated by microvascular damage due to COVID-19.<sup>17</sup>

In summary, potential mechanisms that may increase susceptibility to COVID-19 in patients with diabetes include the following: higher affinity cellular binding and the virus' efficient entry; decreased viral clearance; decreased T cell function; increased susceptibility to hyperinflammation and cytokine storm syndrome; and the presence of cardiovascular diseases.<sup>24</sup>

Approximately 33% of patients hospitalized for COVID-19 had a diagnosis of diabetes, according to a study of 5,416 patients who required hospitalization.<sup>25</sup>

Another factor that is associated with disease prognosis is the patient's body mass index (BMI), given that overweight and obesity are associated with unfavorable prognosis in patients with diabetes who have been hospitalized for COVID-19.<sup>26</sup>

In addition to the risks that influence patient outcomes during the course of the disease, it is important to know the factors that determine the patient's quality of life, functional status, and persistence of symptoms in the long term after SARS-CoV-2 infection.

The factors that contribute to PCS in patients with diabetes include worsening glycemic levels, sarcopenia, malnutrition, electrolyte disorders, worsening of comorbidities, presence of secondary infections, psychological stress, neuropathy, autonomic dysfunction, and use of corticosteroids.<sup>17</sup>

Furthermore, sequelae due to lung damage (such as pulmonary fibrosis) are more frequent in patients with poorly controlled diabetes, who may have persistent dyspnea requiring supplemental oxygen.<sup>27</sup>

Endocrine manifestations in the setting of post-acute COVID-19 may be consequences of direct viral injury, immunological and inflammatory causes, or iatrogenic complications.<sup>28</sup> The preexisting inflammatory state in diabetes can be exacerbated after COVID-19, causing diverse

symptoms.<sup>17</sup> A diagnosis of diabetic ketoacidosis has been identified even in patients without previous diagnosis of diabetes mellitus, weeks to months after the resolution of COVID-19 symptoms.<sup>29</sup>

In diabetes, neuropathy and myopathy contribute to muscle atrophy and sarcopenia.<sup>30</sup> Additionally, factors such as COVID-19 infection, hospitalization, protein deficiency, and corticosteroid therapy often cause rapid onset of sarcopenia in severe COVID-19 infections.<sup>31</sup>

Therefore, the objective of the study was to evaluate manifestations in patients recovered from COVID-19, comparing diabetic and non-diabetic individuals, describing the findings through health instruments: Post-COVID-19 Functional Status (PCFS), EuroQol 5 Dimensions 5 Levels (EQ-5D-5L).

## 2 Material and Methods

### 2.1 Study design

This was a prospective observational study that followed two groups of patients after hospital discharge: with diabetes mellitus or pre-diabetes and without diabetes, with in-person data collection that took place in 2 assessments during the period from August 2020 to December 2022.

### 2.2 Ethics statement

This study research project was submitted and received approval from the Human Research Ethics Committee from Universidade Federal de Santa Catarina (CAAE: 36944620.5.1001.0121) under protocol number 4.290.578. It followed all the ethical standards contained in Resolution CNS n° 466/12, and all participants involved in the study signed a free and informed consent form.

### 2.3 Participants and study location

Treated patients with a positive laboratory diagnosis for COVID-19 were eligible to participate in this study. The inclusion criteria were as follows: patients who required hospitalization, presented moderate or severe form of the disease, and were overweight or obese. The exclusion criteria were patients with BMI > 50 kg/m<sup>2</sup> and assessment conducted outside the convalescence period, established at between 11 and 13 months.

Data were collected during the period from August 2020 to December 2022 in a university hospital located in the South Region of Brazil. The patients involved in the study were assessed at 2 different moments, 73 and 376 days after the beginning of convalescence, respectively. During these assessments, the following health status assessment instruments were applied: Post-COVID-19 Functional Status (PCFS), EuroQol 5 Dimensions 5 Levels (EQ-5D-5L), and visual analog scale (VAS). Patients diagnosed with diabetes and pre-diabetes were considered in the same group for comparison with non-diabetic participants, with the objective

of analyzing the post-COVID-19 clinical repercussions in these 2 patient groups.

## 2.4 Assessment instruments

### 2.4.1 post-COVID-19 Functional Status (PCFS)

The purpose of the PCFS scale is to monitor post-COVID-19 patients' recovery after hospital discharge and assess long-term functional sequelae.<sup>33</sup>

The instrument contains 5 items that grade the patient's functional limitation after COVID-19. The score ranges from 0 to 4, with the maximum score representing the most severe functional limitation. The following items are assessed: constant care; basic activities of daily living; instrumental activities of daily living; participation in usual social roles; and a checklist of symptoms.

### 2.4.2 EuroQol 5 Dimensions-5 Levels (EQ-5D-5L/VAS)

The instrument assesses the following 5 domains: mobility; self-care; usual activities; pain/discomfort; and anxiety/depression. Scores range from 1 to 5, with the minimum score representing no problem and the maximum score representing extreme problems. The visual analog scale (VAS) was used for patients to score their quality of life from 0 (worst imaginable health) to 100 (best imaginable health) at the time of the first and second assessments.<sup>34</sup> Based on its usefulness, it is a widely used instrument, and its validity and reliability have been established.<sup>35</sup>

## 2.5 Statistical analysis

The data collected were tabulated and audited in a Microsoft Excel® spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS), version 23. The normality of the numerical variables was tested using the Shapiro-Wilk test, and they were shown as measures of central tendency and dispersion, whereas categorical variables were shown as absolute and relative frequency. To test the association between categorical variables of interest, the chi-square or Fisher's exact test was used. To compare the numerical variable between categorical variables of interest, the Mann-Whitney U and Kruskal-Wallis tests were used. The level of statistical significance was set at 5%.

## 3 Results and Discussion

During the first assessment, 53 patients were evaluated. Their mean age was 51 years (standard deviation [SD] = 12) years; the mean BMI was 31.2 (29.0 – 34.4) kg/m<sup>2</sup>, and there were 27 women (50.9%). During the second assessment, 52 patients participated, and the mean age was 49 years (SD = 12); the mean BMI was 32.0 (29.8 – 34.8) kg/m<sup>2</sup>, and there were 26 women (50.0%).

Table 1 shows the general characteristics of the study participants. Assessments 1 and 2 occurred 73 (66 – 80)

and 376 (SD = 8) days after the onset of convalescence, respectively.

**Table 1** – Clinical characteristics of the study participants

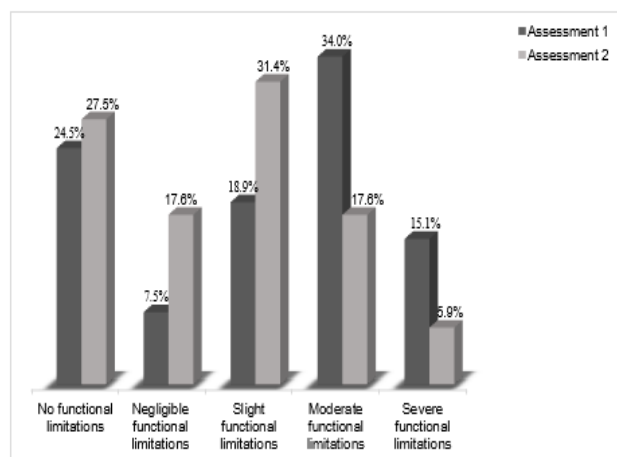
	Assessment 1	Assessment 2
	n (%)	n (%)
<b>ICU</b>		
No	13 (24.5)	6 (11.5)
Yes	40 (75.5)	46 (88.5)
<b>IMV</b>		
No	18 (34.0)	12 (23.1)
Yes	35 (66.0)	40 (76.9)
<b>Obesity</b>		
No	16 (30.2)	16 (30.8)
Yes	37 (69.8)	36 (69.2)
<b>DM</b>		
No	34 (64.2)	35 (67.3)
Yes	19 (35.8)	17 (32.7)

Legend – ICU: intensive care unit; IMV: invasive mechanical ventilation; DM: diabetes mellitus.

Source: research data.

In the first assessment, 19 (35.8%) patients had diabetes, and 37 (69.8%) patients had a diagnosis of obesity, whereas, in the second assessment, 17 (32.6%) of the participants had a diagnosis of diabetes, and 36 (69.2%) participants were obese. Among the 19 patients with diabetes in the first assessment, 15 (78.9%) of them were obese; in the second assessment, among the 17 patients with diabetes, 14 (82.4%) were obese. In the first and second assessments of functional status, the PCFS score was 2 (1 – 3) and 2 (0 – 2), respectively, with 40 (75.5%) and 37 (72.5%) of the participants presenting very mild, mild, moderate, or severe functional limitations (score  $\geq$  1). Figure 1 details the frequency of each PCFS item on both assessments.

**Figure 1** – Distribution of PCFS items



Legend – PCFS: Post-COVID-19 Functional Status. Note: Assessment 1 (n = 53); assessment 2 (n = 51).

Source: research data.

Quality of life was assessed using the EQ-5D-5L. In the first assessment, participants who had moderate, severe, or extreme problems (score  $\geq$  2) in each domain were distributed as follows: 21 (39.6%) in “mobility,” 9 (17.0%) in “self-care,” 24 (45.3%) in “usual activities,” 39 (73.6%) in “pain/discomfort,” and 38 (71.7%) in “anxiety/depression.” In the second assessment, participants with this presentation were distributed as follows: 18 (34.6%) in “mobility,” 5 (9.6%) in “self-care,” 19 (37.3%) in “usual activities,” 38 (73.1%) in “pain/discomfort,” and 34 (65.4%) in “anxiety/depression.” Another study, including 91 patients assessed 6 months after admission to the intensive care unit, demonstrated decreased quality of life in 67% of the participants. Mobility was the most affected domain (56%), followed by pain/discomfort (48%) and anxiety/depression (46%).<sup>36</sup> The results of their study are similar to ours, which also showed that these domains were the most impaired.

VAS, in turn, was equal to 70 [50 – 90] and 80 [60 – 90] in assessments 1 and 2, respectively. No difference was observed in VAS when comparing patients: with and without diabetes mellitus; with and without obesity; without diabetes mellitus or obesity, without diabetes mellitus and with obesity, with diabetes mellitus and without obesity, and with diabetes mellitus and obesity. Regarding VAS, we did not observe a significant difference between patients with and without diabetes. Another study also demonstrated impaired quality of life in 143 patients, 44.1% of whom presented worsened quality of life, verified by VAS score. The scale was applied a mean of 36.1 days after discharge and retrospectively compared with quality of life prior to COVID-19 diagnosis.<sup>3A</sup> A cohort of 78 patients showed that 51% had impaired quality of life, with a mean of 13 weeks after the onset of COVID-19 symptoms, and this finding was similar in patients with and without comorbidities,<sup>37</sup> which corroborates our results, in which there were no differences between the groups with and without diabetes.

The presence or absence of diabetes mellitus was not associated with the items in the EQ-5D-5L domains of “mobility” (assessment 1:  $\chi^2$  [3] 1.793,  $p = 0.617$ ; assessment 2:  $\chi^2$  [3] 2.148,  $p = 0.542$ ), “self-care” (assessment 1:  $\chi^2$  [4] 1.334,  $p = 0.856$ ; assessment 2:  $\chi^2$  [2] 0.286,  $p = 0.867$ ), “usual activities” (assessment 1:  $\chi^2$  [4] 6.516,  $p = 0.164$ ; assessment 2:  $\chi^2$  [4] 4.670,  $p = 0.323$ ), “pain/discomfort” (assessment 1:  $\chi^2$  [4] 3.401,  $p = 0.493$ ; assessment 2:  $\chi^2$  [4] 2.032,  $p = 0.730$ ), and “anxiety/depression” (assessment 1:  $\chi^2$  [4] 6.121,  $p = 0.190$ ; assessment 2:  $\chi^2$  [4] 2.578,  $p = 0.631$ ) in the total sample. This difference in mobility



could be influenced by sarcopenia (Table 2).

**Table 2** – Association between EQ-5D-5L domains and DM in the total sample

	Assessment 1			Assessment 2		
	Without DM	With DM	p value	Without DM	With DM	p value
<b>Mobility</b>						
< 2	19 (55.9)	13 (68.4)	0.40	23 (65.7)	11 (64.7)	1.00
≥ 2	15 (44.1)	6 (31.6)		12 (34.3)	6 (35.3)	
<b>Self-care</b>						
< 2	28 (82.4)	16 (84.2)	1.00	32 (91.4)	15 (88.2)	1.00
≥ 2	6 (17.6)	3 (15.8)		3 (8.6)	2 (11.8)	
<b>Usual activities</b>						
< 2	20 (58.8)	9 (47.4)	0.57	22 (62.9)	10 (62.5)	1.00
≥ 2	14 (41.2)	10 (52.6)		13 (37.1)	6 (37.5)	
<b>Pain/discomfort</b>						
< 2	7 (20.6)	7 (36.8)	0.22	8 (22.9)	6 (35.3)	0.51
≥ 2	27 (79.4)	12 (63.2)		27 (77.1)	11 (64.7)	
<b>Anxiety/depression</b>						
< 2	10 (29.4)	5 (26.3)	1.00	10 (28.6)	8 (47.1)	0.22
≥ 2	24 (70.6)	14 (73.7)		25 (71.4)	9 (52.9)	

Legend – EQ-5D-5L: EuroQol 5 Dimensions 5 Levels; DM: diabetes mellitus. Note: Results expressed as absolute and relative numbers.

Source: research data.

The EQ-5D-5L showed that the most frequent problems reported in our study were pain/discomfort (73.6% and 73.1% in assessments 1 and 2, respectively) and anxiety/depression (71.7% and 65.4% in assessments 1 and 2, respectively). The study by Akter et al.<sup>38</sup> investigated patient complications 4 weeks after recovery from COVID-19, and the most affected domain was pain/discomfort (29.8%). In their study, however, patients with diabetes (40%) had significantly higher levels of pain than those without diabetes (27.3%); furthermore, mobility problems were found to be significantly greater in patients with diabetes than in those without diabetes.<sup>38</sup> In our study, the variable diabetes mellitus was not associated with mobility scores; however, the assessment times were around 2 months (assessment 1) and 1 year (assessment 2)

after hospital discharge, which may suggest that mobility impairment mainly occurs in an earlier phase after hospital discharge (4 weeks).

PCFS scores were not associated with diabetes mellitus (assessment 1:  $\chi^2$  [4] 1.339,  $p = 0.855$ ; assessment 2:  $\chi^2$  [4] 4.240,  $p = 0.374$ ) or obesity (assessment 1:  $\chi^2$  [4] 1.006,  $p = 0.909$ ; assessment 2:  $\chi^2$  [4] 3.208,  $p = 0.524$ ), even when they were pooled (assessment 1:  $\chi^2$  [12] 4.666,  $p = 0.968$ ; assessment 2:  $\chi^2$  [12] 15.146,  $p = 0.234$ ) (Table 3). When the PCFS scores were dichotomized, the lack of association with diabetes, obesity, and pooled diabetes mellitus and obesity was maintained.

**Table 3** – Association of DM and/or obesity with PCFS

PCFS	Without DM or obesity	Without DM and with obesity	With DM and without obesity	With DM and obesity	p value
<b>Assessment 1</b>					
< 2	3 (25.0)	7 (31.8)	1 (25.0)	6 (40.0)	0.85
≥ 2	9 (75.0)	15 (68.2)	3 (75.0)	9 (60.0)	
<b>Assessment 2</b>					
< 2	6 (46.2)	7 (31.8)	2 (66.7)	8 (61.5)	0.31
≥ 2	7 (53.8)	15 (68.2)	1 (33.3)	5 (38.5)	

Legend –DM: diabetes mellitus; PCFS: Post-COVID-19 Functional Status. Note: Results expressed as absolute and relative numbers.

Source: research data.

This difference in mobility could be influenced by sarcopenia. There is evidence that patients with diabetes have an increased risk of sarcopenia compared to those without diabetes.<sup>30</sup> Nonetheless, limitations in mobility and in other domains have been observed in both groups, showing the impact of the disease on the lives of patients both with and without a diagnosis of diabetes.

Our study found a very homogeneous group of patients, which may be one of the causes for this difference not being significant between the groups of patients with and without diabetes. Other limitations are due to the sample size and the fact that all patients were hospitalized, in a ward and/or intensive care unit, which may be factors that make it difficult to generalize the results to other patient groups. The relatively low mean age of the patients (51 years) may have influenced the result, given that elderly patients are known to have lower scores on the EQ-5D.<sup>39,40</sup>

In the group of patients without diabetes, other comorbidities were present in 19 of the 34 patients (55.9%) and 16 of the 35 patients (45.7%) in the first and second assessments, respectively, which may have interfered with the lack of significant difference between the groups analyzed, given that chronic diseases can influence the quality of life

score.<sup>41</sup> Other study limitations include the absence of a control group (patients without comorbidities) and the lack of data about patients' quality of life and functionality during the pre-COVID-19 period. In the group of patients with diabetes, 84.2% and 70.6%, in assessments 1 and 2, respectively, had other comorbidities, making it difficult to assess the influence of diabetes alone on the patients' quality of life. Our study also did not include a control group without COVID-19 to differentiate specific effects mediated by COVID-19 from those mediated by critical illnesses.

Our study was conducted in person with the participants; furthermore, during the assessments, we asked about medication use and comorbidities, and we filled out the Charlson Comorbidity Index for all participants.

The PCFS scores were not associated with diabetes. When the PCFS scores were dichotomized, the lack of association with diabetes mellitus, obesity, and pooled diabetes mellitus and obesity was maintained.

A case-control study, which assessed post-COVID-19 patients with and without diabetes a mean of 7 months after hospital discharge, verified that diabetes was not associated with differences in limited activities of daily living,<sup>42</sup> which corroborates our results.

In assessments 1 and 2, respectively, 36 (67.9%) and 28 (54.9%) study participants presented slight, moderate, or severe functional limitation (score  $\geq 2$ ). This result is in agreement with another study including 91 patients, which showed that 63% reported decreased functional status 6 months after hospitalization; however, in that study, all participants had been admitted to an intensive care unit.<sup>36</sup>

There are some limitations to defining which factors interfere with the impact that COVID-19 will have on patients' quality of life in the long term, because there are few studies with follow-up of patients for 12 months. It is also necessary to consider sociodemographic and clinical factors in order to better define the impact of PCS and distinguish it from confounding factors related to this condition.<sup>43</sup>

Although it is difficult to determine the exact epidemiological data about PCS, this information is necessary to assist health systems and governments so that they can develop appropriate support plans and treatments.<sup>44</sup>

The patients included in our study represent a small sample of the population hospitalized for COVID-19; however, considering that 537 million people have been diagnosed with diabetes worldwide (10.5% of the world population),<sup>45</sup> and if we project the impact on these patients' lives and the limitations to daily living, these results may be an alert regarding the implementation of public health policies in order to prevent the consequences of PCS.

Sedentary behavior has been an important patient complaint during the pandemic; for this reason, approaches such as telerehabilitation are beneficial for increasing physical activity; improving quality of life; and decreasing anxiety, depression, and perceived loneliness during the pandemic

period for all the individuals, as shown by a study including patients with type 1 diabetes and a control group.<sup>46</sup>

Multidisciplinary rehabilitation teams should provide support to these patients by addressing the physical, psychological, and psychiatric aspects of rehabilitation, and managing the complaint of fatigue should be the key component.<sup>47</sup>

The stratification of patients' limitations can be a means to organize support so that each patient receives treatment with specialized teams, with a multidisciplinary approach including nutritional, physical therapy, and psychological follow-up.<sup>17</sup>

## 4 Conclusion

Based on the results of our study, we conclude that diabetes does not seem to interfere with patients' quality of life and functionality during a 1-year period after hospitalization for COVID-19. The main complaints were in the domains of pain/discomfort and anxiety/depression; furthermore, more than 60% of patients presented functional limitations with PCFS  $\geq 2$  approximately 2 months after hospitalization for COVID-19, in both the groups with and without diabetes. To improve these patients' quality of life and functionality, outpatient follow-up for the treatment of PCS should have a multidisciplinary approach.

## References

1. COVID-19 rapid guideline: managing the long-term effects of COVID-19. London: National Institute for Health and Care Excellence (NICE); 2020.
2. Iqbal FM, Lam K, Sounderajah V, Clarke JM, Ashrafian H, Darzi A. Characteristics and predictors of acute and chronic post-COVID syndrome: A systematic review and meta-analysis. *Eclin Med* 2021;36:100899. doi: 10.1016/j.eclinm.2021.100899.
3. Carfi A, Bernabei R, Landi. Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020;324(6):603-5. doi: 10.1001/jama.2020.12603.
4. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. *Nat Med*. 2021;27(4):626-631. Erratum in: *Nat Med* 2021;27(6):1116. doi: 10.1038/s41591-021-01292-y.
5. Feldman EL, Savelieff MG, Hayek SS, Pennathur S, Kretzler M, Pop-Busui R. COVID-19 and diabetes: a collision and collusion of two diseases. *Diabetes* 2020;69(12):2549e65. doi: <https://doi.org/10.2337/dbi20-0032>.
6. Carvalho-Schneider C, Laurent E, Lemaigen A, Beauflis E, Bourbao-Tournois C, Laribi S, et al. Follow-up of adults with noncritical COVID-19 two months after symptom onset. *Clin Microbiol Infect* 2021;27(2):258-263. doi: 10.1016/j.cmi.2020.09.052.
7. Evans RA, McAuley H, Harrison EM, Shikotra A, Singapuri A, Sereno M, et al. Physical, cognitive, and mental health impacts of COVID-19 after hospitalisation (PHOSP-COVID): a UK multicentre, prospective cohort study. *Lancet*

- Respir Med 2021;9(11):1275-87. doi: 10.1016/S2213-2600(21)003830.
8. Han Q, Zheng B, Daines L, Sheikh A. Long-Term Sequelae of COVID-19: a systematic review and meta-analysis of one-year follow-up studies on post-COVID symptoms. *Pathogens* 2022;11(2):269. doi: 10.3390/pathogens11020269.
  9. Stavem K, Ghanima W, Olsen MK, Gilboe HM, Einvik G. Prevalence and determinants of fatigue after COVID-19 in non-hospitalized subjects: a population-based study. *Int J Environ Res Public Health* 2021;18(4):2030. doi: 10.3390/ijerph18042030.
  10. Goërtz YMJ, Van Herck M, Delbressine JM, Vaes AW, Meys R, Machado FVC, et al. Persistent symptoms 3 months after a SARS-CoV-2 infection: the post-COVID-19 syndrome? *ERJ Open Res* 2020;26(6(4):00542-2020. doi: 10.1183/23120541.00542-2020.
  11. D'Cruz RF, Waller MD, Perrin F, Periselneris J, Norton S, Smith LJ, et al. Chest radiography is a poor predictor of respiratory symptoms and functional impairment in survivors of severe COVID-19 pneumonia. *ERJ Open Res* 2021;7(1):00655-2020. doi: 10.1183/23120541.00655-2020.
  12. Townsend L, Dyer AH, Jones K, Dunne J, Mooney A, Gaffney F et al. Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. *PLoS One* 2020;15(11):e0240784. doi: 10.1371/journal.pone.0240784.
  13. Huang C, Huang L, Wang Y, Li X, Ren L, Gu X, et al. 6-Month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021;397(10270):220-32. doi: 10.1016/S0140-6736(20)32656-8.
  14. Azzolini E, Levi R, Sarti R, Pozzi C, Mollura M, Mantovani A, et al. Association between BNT162b2 vaccination and long COVID after infections not requiring hospitalization in health care workers. *JAMA* 2022:e2211691.
  15. Chen C, Hauptert SR, Zimmermann L, Shi X, Fritsche LG, Mukherjee B. Global prevalence of post COVID-19 condition or long COVID: a meta-analysis and systematic review. *J Infect Dis* 2022;jiac136. doi: <https://doi.org/10.1093/infdis/jiac136>.
  16. Unnikrishnan R, Misra A. Diabetes and COVID19: a bidirectional relationship. *Eur J Clin Nutr* 2021;75(9):1332-6. doi: 10.1038/s41430-021-00961-y.
  17. Raveendran A.V, Misra A. Post COVID-19 Syndrome ("Long COVID") and Diabetes: Challenges in Diagnosis and Management. *Diabetes Metab Syndr* 2021;15(5):102235. doi: 10.1016/j.dsx.2021.102235
  18. Misra A, Ghosh A, Gupta R. Heterogeneity in presentation of hyperglycaemia during COVID-19 pandemic: a proposed classification. *Diabetes Metab Syndr* 2021;15(1):403-6. doi: 10.1016/j.dsx.2021.01.018.
  19. de Almeida-Pititto B, Dualib PM, Zajdenverg L, Dantas JR, Souza FD, Rodacki M, et al. Severity and mortality of COVID 19 in patients with diabetes, hypertension and cardiovascular disease: a meta-analysis. *Diabetol Metab Syndr* 2020;12:75. doi: 10.1186/s13098-020-00586-4.
  20. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. *Acta Diabetol* 2010;47(3):193-9. doi: 10.1007/s00592-009-0109-4.
  21. Gentile S, Strollo F, Mambro A, Ceriello A. COVID-19, ketoacidosis and new-onset diabetes: are there possible cause and effect relationships among them? *Diabetes Obes Metab* 2020;22(12):2507-8. doi: 10.1111/dom.14170.
  22. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk for the progression and prognosis of COVID-19. *Diabetes Metab Res Rev* 2020;36(7):e3319. doi: 10.1002/dmrr.3319.
  23. Ceriello A, Standl E, Catrinou D, Itzhak B, Lalic NM, Rahelic D, et al. Issues of cardiovascular risk management in people with diabetes in the COVID-19 Era. *Diabetes Care* 2020;43(7):1427-32. doi: 10.2337/dc20-0941.
  24. Muniyappa R, Gubbi S. COVID-19 pandemic, coronaviruses, and diabetes mellitus. *Am J Physiol Endocrinol Metab* 2020;318(5):36-41. doi: 10.1152/ajpendo.00124.2020.
  25. Ko JY, Danielson ML, Town M, Derado G, Greenlund KJ, Kirley PD, et al. Risk factors for coronavirus disease 2019 (COVID-19)-associated hospitalization: COVID-19-associated hospitalization surveillance network and behavioral risk factor surveillance system. *Clin Infect Dis* 2021;72(11):e695-e703. doi: 10.1093/cid/ciaa1419.
  26. Smati S, Tramunt B, Wargny M, Caussy C, Gaborit B, Vatier C, et al. Relationship between obesity and severe COVID-19 outcomes in patients with type 2 diabetes: Results from the CORONADO study. *Diab Obes Metab* 2021;23(2):391-403. doi: 10.1111/dom.14228.
  27. Mrigpuri P, Sonal S, Spalgais S, Goel N, Menon B, Kumar R. Uncontrolled diabetes mellitus: a risk factor for post COVID fibrosis. *Monaldi Arch Chest Dis* 2021;91(1). doi: 10.4081/monaldi.2021.1607.
  28. Nalbandian A, Sehgal K, Gupta A, Madhavan MV, McGroder C, Stevens JS, et al. Post-acute COVID-19 syndrome. *Nat Med* 2021;27(4):601-15. doi: 10.1038/s41591-021-01283-z.
  29. Suwanwongse, K. Shabarek, N. Newly diagnosed diabetes mellitus, DKA, and COVID-19: causality or coincidence? A report of three cases. *J Med Virol* 2020;93(2):1150-3. doi: 10.1002/jmv.26339.
  30. Anagnostis P, Gkekas NK, Achilla C, Pananastasiou G, Taoukidou P, Mitsiou M, et al. Type 2 diabetes mellitus is associated with increased risk of sarcopenia: a systematic review and meta-analysis. *Calcif Tissue Int* 2020;107(5):453-63. doi: 10.1007/s00223-020-00742-y.
  31. Welch C, Greig C, Masud T, Wilson D, Jackson TA. COVID-19 and Acute Sarcopenia. *Aging Dis* 2020;11(6):1345-51. doi: 10.14336/AD.2020.1014.
  32. NIH COVID-19 guidelines- "Clinical Spectrum of SARS-CoV-2 Infection". [access 8 abr 2024]. Available at <https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/>
  33. Klok FA, Boon GJAM, Barco S, Endres M, Geelhoed JJM, Knauss S, et al. The Post-COVID-19 Functional Status scale: a tool to measure functional status over time after COVID-19. *Eur Respir J* 2020;56(1):2001494. doi: 10.1183/13993003.01494-2020.

34. EuroQol Research Foundation, EQ-5D-5L user guide. [assessed 10 apr 2024]. Available at: <https://euroqol.org/publications/user-guides>.
35. Janssen MF, Lubetkin EI, Sekhobo JP, Pickard AS. The use of the EQ-5D preference-based health status measure in adults with Type 2 diabetes mellitus. *Diabet Med* 2011;28(4):395-413. doi: <https://doi.org/10.1111/j.1464-5491.2010.03136.x> PMID: 21392061
36. Taboada M, Moreno E, Cariñena A, Rey T, Pita-Romero R, Leal S, et al. Quality of life, functional status, and persistent symptoms after intensive care of COVID-19 patients. *Br J Anaesth* 2021;126(3):e110-e3. doi: 10.1016/j.bja.2020.12.007.
37. Wong AW, Shah AS, Johnston JC, Carlsten C, Ryerson CJ. Patient-reported outcome measures after COVID-19: a prospective cohort study. *Eur Respir J* 2020;56(5):2003276. doi: 10.1183/13993003.03276-2020.
38. Akter F, Mannan A, Mehedi HMH, Rob MA, Ahmed S, Salauddin A, et al. Clinical characteristics and short-term outcomes after recovery from COVID-19 in patients with and without diabetes in Bangladesh. *Diabetes Metab Syndr* 2020;14(6):2031-8. doi: 10.1016/j.dsx.2020.10.016
39. Fujikawa A, Suzue T, Jitsunari F, Hirao T. Evaluation of health-related quality of life using EQ-5D in Takamatsu, Japan. *Environ Health Prev Med* 2011;16(1):25-35. doi: 10.1007/s12199-010-0162-1.
40. Kind P, Dolan P, Gudex C, Williams A. Variations in population health status: results from a United Kingdom national questionnaire survey. *BMJ* 1998;316(7133):736-41. doi: 10.1136/bmj.316.7133.736.
41. Ping W, Zheng J, Niu X, Guo C, Zhang J, Yang H, et al. Evaluation of health-related quality of life using EQ-5D in China during the COVID-19 pandemic. *PLoS One* 2020;15(6):e0234850. doi: 10.1371/journal.pone.0234850.
42. Fernández-de-Las-Peñas C, Guijarro C, Torres-Macho J, Velasco-Arribas M, Plaza-Canteli S, Hernández-Barrera V, et al. Diabetes and the risk of long-term post-COVID symptoms. *Diabetes* 2021;70(12):2917-21. doi: 10.2337/db21-0329.
43. d'Ettorre G, Vassalini P, Coppolelli V, Gentilini Cacciola E, Sanitinelli L, et al. Health-related quality of life in survivors of severe COVID-19 infection. *Pharmacol Rep* 2022;74(6):1286-95. doi: 10.1007/s43440-022-00433-5.
44. Crook H, Raza S, Nowell J, Young M, Edison P. Long covid-mechanisms, risk factors, and management. *BMJ* 2021;374:1648. doi: 10.1136/bmj.n1648. Erratum in: *BMJ* 2021;374(1944).
45. International Diabetes Federation (IDF). IDF Diabetes Atlas. 2021. Available at: <https://www.diabetesatlas.org>.
46. Çelik Z, Törüner FB, Güçlü MB. Evaluation of quality of life and physical activity in patients with type 1 diabetes mellitus during the COVID-19 pandemic. *Arch Endocrinol Metab* 2023; 67(2):206-13. doi: 10.20945/2359-3997000000531.
47. Shah W, Hillman T, Playford ED, Hishmeh L. Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. *BMJ* 2021;372:n136. doi: 10.1136/bmj.n136. Erratum in: *BMJ*. 2022 Jan 19;376:o126.