

# Patient-reported outcomes measures after six months of COVID-19: Impacts on health-related quality of life

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## Abstract

**Aim:** To evaluate health-related quality of life (HRQOL) outcomes after discharge from the perspective of the patient recovered from COVID-19 in Brazil.

**Methods:** A prospective follow-up was performed during 180 days after hospital discharge in diagnosed patients with COVID-19 (by RT-qPCR) from June to September 2020. Standard scales were used to measure outcomes through the patient's perception. Paired analyses were performed for individuals that completed the questionnaire in the corresponding follow-up periods.

**Results:** 270 patients were admitted to the hospital. Of the total, 236 were followed up after discharge, 10 refused (3.7%) to participate in the program and 24 (8.8%) died during hospitalization. The HRQOL was investigated in 146 patients. We identified a gradual improvement over time after hospital discharge, except for the anxiety/depression domain. Evaluation by domains of mobility, self-care, usual activities and pain frequencies improved in 180 days.

**Conclusion:** We demonstrate the importance of following up after discharge patients hospitalized by COVID-19, mainly by the psychological effects caused. Prospective follow-up studies will help comprehend the pathogenesis and its long-term impact, providing real-world data that will support decision-making.

**Keywords:** COVID-19; coronavirus; health-related quality of life; PROMS.

## HIGHLIGHTS

- On hospital admission, the most frequently reported symptoms were fever (63.0%), cough (59.5%), dyspnea (43.1%) and myalgia (30.8%).
- The first study to perform a prospective study of HRQOL in Brazilian inpatients with COVID-19.
- Our results found improvement in 180 days after hospital discharge in all EQ5D domains, except for anxiety/depression.

## INTRODUCTION

The coronavirus disease 19 (COVID-19) caused by a novel etiological agent<sup>1</sup> is an emerging health problem declared by The World Health Organization (WHO), which first appeared in Wuhan, Hubei Province, China<sup>2</sup>. Until April, 2021, the rapid spread of the virus had caused more than 10.000.000 cases and 300.000 deaths in Brazil<sup>3</sup>.

Symptoms and long-term effects experienced by survivors of COVID-19 after discharge from hospital are unknown. Studies in recovered patients to

determine their health status and other detrimental conditions are needed<sup>4</sup>. Long-term repercussions will be important to determine potential complications as well as providing information about the pathogenesis and prognosis. Patient-reported outcome measures (PROMs) are standardized validated questionnaires that patients use to provide information on aspects of their health status and quality of life, including symptoms, functionality, and physical, mental and social health.<sup>5</sup> PROMs play an important role in improving health systems and ensuring that clinical care and research is person-centered.<sup>6</sup>

Here, we describe a single-centre study assessing post-discharge outcomes of health-related quality-of-life (HRQOL) from the recovered COVID-19 patient's perspective in a reference Brazilian hospital. Our main aims were to describe and analyze real-world data associated with the impact of the COVID-19 pandemic that can support decision-making.

### METHODS

The Clinical Outcomes Program from Value Management Office (VMO) at Moinhos de Vento Hospital followed inpatients diagnosed with COVID-19 (by RT-qPCR) from June to September, 2020. The Clinical Outcomes Program uses assessments of clinical outcomes (patient reported, clinician reported, observational reported, and performance outcomes) and encourages harmonization among all stakeholders of interest.

A prospective cohort was follow-up on day 7, 14, 30, 90 and day 180 after hospital discharge. General Anxiety Disorder scale (GAD7), Lawton-Brody scale, EuroQol five-dimensional (EQ5D-3L) and EuroQol visual analog scale (EQVAS) are validated instruments in the Portuguese language and were used as outcome measures of HRQOL. Scores for GAD7 are interpreted as a range 0 to 21 where: 0-4 points is equal to minimal anxiety; 5-9 points mild anxiety; 10-14 points moderate anxiety and >15 points severe anxiety. The Lawton-Brody scale summary score ranges from 0 points (low function, dependent) to 8 points (high function, independent) for women and 0 through 5 for men to avoid potential gender bias. EQ5D-3L summary index score range -0.176 a 1.0 where 1.0 represents the best possible health status. The VAS is part of the EQ-5D, mentioned as a health status thermometer, ranging from 0 to 100 for the patients to evaluate their current general health status; 0 represents the

possible worst health status and the 100 represents the best possible health status.

The minimal clinical important difference (MCID), representing the magnitude of change that is clinically meaningful to patients was estimated by Bae et al (2020) and Zanini (2015). The MCID estimated for EQ5D was 0.028 and 8 points for EQVAS, from a sample of patients with chronic obstructive pulmonary disease. After thorough review we chose to use this standard since there are no MCID studies for COVID-19. For this purpose, we calculate the difference between the last and the first visit (day 180 - day 7).

Paired analyses were performed for individuals that completed the questionnaire in the corresponding follow-up periods. Clinical data, including comorbidities, symptoms and details of hospitalization were obtained from electronic records. The Ethics Committee approved this study (CAEE: 30350820.5.2037.5330).

### RESULTS

From June to September 2020, 270 patients were admitted to the hospital. Of the total, 236 were followed up after discharge, 10 refused (3.7%) to participate in the program and 24 (8.8%) died during hospitalization. The HRQOL was investigated in 146 patients (58.2% male) with a median age of 60 years (IQR, 45.0-72.0 years). On hospital admission, the most frequently reported symptoms were fever (63.0%), cough (59.5%), dyspnea (43.1%) and myalgia (30.8%). Hypertension and heart disease were seen in 48.6% and 19.8% of patients, respectively. Depression was reported for 8.2% patients. Of all patients 12.8% had  $\geq 50\%$  compromise lung, 14.2% were admitted in intensive care units (ICU) and 8.2% needed invasive ventilatory support with median of stay to 7.5 days (IQR 3.5-19.0).

We evaluated HRQOL results in functional and psychological domains of inpatients with COVID-19. One week after discharge, 18.49% and 4.11% had moderate (10-14 points) or severe GAD ( $\geq 15$  points), respectively. Differences among the visits were observed when comparing day 7 with day 30 ( $p < .0001$ ) with a decrease in the severe group. Nevertheless, at 6 months this positive difference was weaker ( $p=0.05$ ). For regular activities, measured by the Lawton-Brody scale, there was a significant improvement in all times after discharge ( $p < 0.0001$ ), reaching a mean of 7.3 points in 180 days, where 8.0 points equals total independence.

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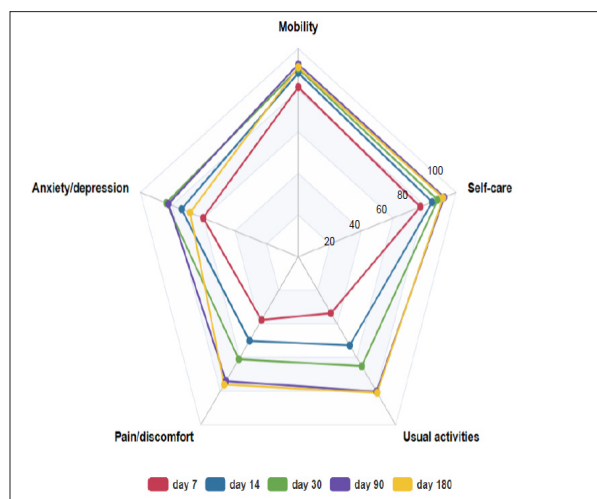
We identified a EQ5D global score of 0.754 (SD±0.21) and VAS score 81.02 (SD±1.2). In 180 days, EQ5D index score was 0.837 (SD±0.20) and 87.0 points for VAS (SD±11.1), significantly better compared to day 7 (p<.0001). Analyzing by domains, the group reporting no problems increased over time, except for the

anxiety domain, which improved in frequency up to 90 days but decreased 13.7% on day 180. According to the MCID calculation, for the EQ5D index 73.9% (108) and for EQVAS 60.2% (88) improved their results at the end of the follow-up. HRQOL scores are summarized in Table 1.

**Table1.** HRQOL scores of 146 patients.

	% or mean (SD)					P value
	7 days	14 days	30 days	90 days	180 days	
<b>No problems<sup>1</sup></b>						
Mobility	81.5	88.3	90.4	92.4	91.1	
Self-care	77.4	84.9	88.3	92.4	91.7	
Usual activities	33.5	52.7	65.0	80.1	80.8	
Pain/discomfort	37.6	50.0	60.9	73.9	76.0	
Anxiety/depression	60.2	73.9	83.5	82.1	68.4	
<b>Some problems<sup>2</sup></b>						
Mobility	15.0	9.5	7.5	6.1	7.5	
Self-care	15.7	10.9	9.5	6.8	5.4	
Usual activities	58.2	43.8	33.5	18.4	16.4	
Pain/discomfort	55.4	48.6	38.3	22.6	21.2	
Anxiety/depression	34.9	19.8	14.3	14.3	21.2	
<b>Problems<sup>2</sup></b>						
Mobility	3.4	2.0	2.0	1.3	1.3	
Self-care	6.8	4.1	2.0	0.6	2.7	
Usual activities	8.2	3.4	1.3	1.3	2.7	
Pain/discomfort	6.8	1.3	0.6	3.4	2.7	
Anxiety/depression	4.7	6.1	2.0	3.4	10.2	
<b>EQ5D-3L index<sup>a</sup></b>	0.668 (0.22)	0.762 (0.20)*	0.819 (0.20)*	0.866 (0.19)*	0.837 (0.20)*	p <.0001*
<b>VAS<sup>b</sup></b>	77.5 (11.5) <sup>β</sup>	83.3 (10.1) <sup>β</sup>	87.8 (9.5) <sup>β</sup>	89.5 (9.5) <sup>β</sup>	87.0 (11.1) <sup>β</sup>	p <.0001 <sup>β</sup>
<b>LAWTON-BRODY<sup>c</sup></b>	6.2 (2.2) <sup>†</sup>	6.8 (1.9) <sup>†</sup>	7.2 (1.7) <sup>†</sup>	7.4 (1.5) <sup>†</sup>	7.3 (1.7) <sup>†</sup>	p <.0001 <sup>†</sup>
<b>GAD7<sup>d</sup></b>	4.1 (5.1)	3.4 (5.0)	2.1 (4.0) <sup>α</sup>	2.4 (4.5) <sup>α</sup>	3.2 (5.3)	p <.0001 <sup>α</sup>

\*α † and β comparative day 7-14, 7-30, 7-90 and day 7-180; For a better quality of life values should increase<sup>1</sup> or decrease<sup>2</sup> with the course of time. <sup>a</sup>Summary score, ranging from -0.176 to 1.0 (best imaginable health). <sup>b</sup>EuroQol visual analog scale, ranging from 0 to 100 (best imaginable health). <sup>c</sup>Lawton-Brody scale, ranging from 0 (dependent) to 8 (independent). <sup>d</sup>GAD7 score, 0-4 minimal anxiety; 5-9 mild anxiety; 10-14 moderate anxiety; >15 severe anxiety.



**Fig1.** HRQOL EQ5D-3L domains

## DISCUSSION

To our knowledge, this is the first study to perform a prospective study of HRQOL in Brazilian inpatients with COVID-19. According to the response rate “I have no problem” for each domain, this study found an improvement in 180 days after hospital discharge in all EQ5D domains, except for anxiety/depression (Figure 1). The absence of improvement in the anxiety/depression status highlights the importance of a specific follow-up of these patients, guiding cases that require psychological or psychiatric intervention. Psychiatric outcomes will also be evaluated in this population.

Our EQ5D global score was similar to that found in Chinese population, Ping et al (2020)<sup>7</sup> found a mean score of 0.949 and VAS of 85.52 during the COVID-19 pandemic, data reported by outpatients. An Italian study<sup>8</sup> reported that 60 days after discharge, 44.1% of patients had a worsening quality of life after the disease. Due to the absence of long-term studies in Brazil, there are no comparisons for our population. Limitations of the study include the relatively small number of patients, and the single-center nature of our series.

In conclusion, many symptoms and effects persist months after hospitalization for COVID-19. Prospective follow-up studies are needed and will help comprehend the pathogenesis and its long-term impact, providing real-world data that will support decision-making. Our findings highlight the impact that COVID-19 has on patients even after reported recovery, mainly by the psychological effects caused by the disease. Our perspective is to monitor up to 1 year and our findings must be confirmed in larger cohorts.

## ETHICS APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration

and its later amendments or comparable ethical standards. This study was reviewed and approved by the research ethics committee of the Hospital Moinhos de Vento.

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