

## Factors associated with disability in patients after discharge from Intensive Care Units COVID-19

### Fatores associados à incapacidade de pacientes após alta em Unidades de Terapia Intensiva COVID-19

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**ABSTRACT**

**Objective:** to evaluate factors associated with disability of patients after hospital discharge in COVID-19 intensive care units. **Methods:** cross-sectional analytical research with sociodemographic, clinical, self-perception of health and WHODAS 2.0 scale data of patients discharged from a teaching hospital. Patients admitted to an intensive care unit for COVID-19 for more than eight days, discharged from the hospital at least 365 days before data collection and older than 18 years were included. Information analysis was performed using data mining. **Results:** 32 individuals were eligible, 25% were disabled. These individuals presented low cognition, mobility, self-care, limitation in daily activities, justified by biological and clinical parameters. Still, 37% by obesity and polymedication, 75%, impaired concentration and 50%, neurological developments. The length of hospitalization and the therapeutic resources demanded in this period were also associated with the disability observed. **Conclusion:** the COVID-19 virus added to the length of hospitalization and clinical factors were related to disability 12 months after hospital discharge with strong presence of neurological symptoms. **Contributions to practice:** it is expected to contribute to the understanding of the long-term impacts of COVID-19, enabling to offer better assistance and quality of life to patients affected by the disease. **Descriptors:** COVID-19; International Classification of Functioning, Disability and Health; Intensive Care Units.

**RESUMO**

**Objetivo:** avaliar fatores associados à incapacidade de pacientes após a alta hospitalar em unidades de terapia intensiva COVID-19. **Métodos:** pesquisa transversal analítica com dados sociodemográficos, clínicos, de autopercepção de saúde e escala de WHODAS 2.0 de pacientes egressos de um hospital-escola. Foram incluídos: pacientes internados em unidade de terapia intensiva por COVID-19 por um período de mais de oito dias; com alta hospitalar recebida, no mínimo, 365 dias antes da coleta de dados; maiores de 18 anos. A análise das informações foi realizada por meio de mineração de dados. **Resultados:** foram elegíveis 32 indivíduos, sendo 25% incapacitados. Estes apresentaram baixa cognição, mobilidade, autocuidado, limitação em atividades diárias, justificadas por parâmetros biológicos e clínicos. Ainda, 37% por obesidade e polimedicação, 75%, concentração comprometida e 50%, desdobramentos neurológicos. O tempo de internamento e os recursos terapêuticos demandados neste período também foram associados à incapacidade observada. **Conclusão:** o vírus da COVID-19 somado ao tempo de internação e fatores clínicos foram relacionados à incapacidade 12 meses após alta hospitalar com forte presença de sintomas neurológicos. **Contribuições para a prática:** espera-se contribuir para a compreensão dos impactos em longo prazo da COVID-19, possibilitando oferecer melhor assistência e qualidade de vida aos pacientes acometidos pela doença. **Descritores:** COVID-19; Classificação Internacional de Funcionalidade, Incapacidade e Saúde; Unidade de Terapia Intensiva.

## Introduction

The disease caused by the new coronavirus (COVID-19) was detected at the end of 2019 and gathers millions of cases on all continents and thousands of deaths in Brazil<sup>(1)</sup>, generating an unprecedented panorama of critically ill patients requiring Intensive Care Unit (ICU) treatment at risk of developing long-term damages<sup>(2)</sup>.

Symptoms following ICU admission for COVID-19 may occur in the physical, mental, and cognitive areas, negatively impacting quality of life<sup>(3-5)</sup> due to impaired functioning of the respiratory system<sup>(6)</sup>, gastrointestinal system<sup>(7)</sup>, hematopoietic system, cardiovascular system<sup>(8)</sup>, and central nervous system<sup>(9)</sup>. Classically, there is an association between hospitalization and the development of chronic diseases<sup>(10)</sup> with increased mortality in the months and years following hospital discharge, in addition to higher costs in relation to health services<sup>(11)</sup>.

Specifically about the long-term consequences of patients after hospitalization, although not fully known, the negative outcomes tend to be substantial before the knowledge of risk factors common to egresses from critical care units with shorter duration of treatment<sup>(2,5,12)</sup>.

The medical field has a well-characterized Post-intensive care syndrome (PICS), defined as a set of cognitive, physical (muscle weakness and atrophy) and mental alterations that reduce the individual's quality of life after hospital discharge<sup>(13)</sup>. Frequently, this syndrome is associated with length of hospitalization, presence of brain, respiratory, acute cardiac dysfunction and prolonged antibiotic therapy<sup>(13-14)</sup> with functional sequelae probably more pronounced in patients with COVID-19.

In this sense, research that evaluates the results of prolonged hospitalization on functional aspects is important to provide adequate post-treatment therapies to these patients, considering their physical, mental and cognitive needs. Most published studies evaluated patients up to six months after hospitalization for

the disease, which may make it difficult to interpret the relationship with functionality<sup>(5)</sup>.

The objective of the present study was to evaluate factors associated with disability of patients after hospital discharge in COVID-19 intensive care units.

## Methods

This is a cross-sectional, analytical study with a quantitative approach based on primary and secondary data from patients at the Campos Gerais Regional University Hospital, Paraná, Brazil.

The research subjects were in total 32 (100%) patients discharged from the ICU between March 2020 and March 2021. Inclusion criteria were: having stayed in the hospital ICU for COVID-19; having been discharged from the hospital at least 365 days before the interview; being over 18 years old; having a length of stay longer than eight days, taking as reference the indicators of average length of stay of patients admitted to the General ICU in 2019.

The exclusion criteria were: patients with cognitive impairment (as assessed by the family); uncorrected hearing loss that prevented them from understanding the questions (as assessed by the researcher); with speech impairment (as assessed by the family); with changes in functionality prior to hospitalization for COVID-19; patients who did not answer the phone call after three attempts on different days and times.

Primary data were obtained by means of recorded telephone interviews with the patients themselves, using a new structured instrument containing sociodemographic, clinical and self-perception of health questions and the WHODAS 2.0 scale, 12-item version (administered by an interviewer), translated and validated for the Portuguese language in Brazil. The collection was performed by telephone call by trained researchers with no time limitation for the answers.

The World Health Organization Disability Assessment Schedule (WHODAS 2.0) is a generic assessment instrument developed by the World Health Organization (WHO) to provide a standardized method

for measuring health and disability in the population or clinical setting. The WHODAS 2.0 12-item version assesses activity limitations and participation restrictions across six domains: cognition; mobility; self-care; interpersonal relationships; and activities of living and participation during the 30 days preceding the interview, applying a 5-point scale to all items, where 1 indicates no difficulty and 5 indicates extreme difficulty or inability to do the activity.

The dependent variable was the functionality of the patient, measured by the difficulty presented in the domains of analysis of the WHODAS 2.0 with the response scale for mild, moderate, severe and extreme. The independent variables were sociodemographic (gender; age; education; marital status; family/social arrangement; occupation; personal income; and monthly family income), clinical (chronic diseases; polypharmacy; depression; length of hospitalization; need for mechanical ventilation; need for pronation; cardiac arrest; need for antibiotics; and need for full anticoagulation) and self-perception of general health.

In this study, dimensionality reduction techniques were used prior to the Classification Data Mining step for supervised learning. This dimensionality reduction was accomplished by the Wrapper attribute selection algorithm and the Correlation-based Feature Selection (CFS) algorithm.

The first method obtained the data set related to the classes of a given variable, directed to the characteristics of a specific algorithm. The CFS algorithm, on the other hand, prioritizes sets of independent variables that are more related to the Disability variable and have little relation to each other, decreasing the collinearity of the set of selected variables.

Data mining techniques of supervised and unsupervised learning were used in a Knowledge Discovery in Databases (KDD) process. In the data exploration phase, the Normality Test: Kolmogorov-Smirnov (KS) was used to guide the use of bivariate analysis through parametric and nonparametric tests of variance analysis.

In the Data Mining phase, description tech-

niques were used: clustering and association rules and classification, through algorithms established in the literature, Kmeans, Apriori and J48 respectively. In the Data Mining pre-processing macro stage, 32 records corresponding to 59 variables were submitted to the cleaning stage, which basically consists of standardizing terms, eliminating or correcting noise, and treating missing data. Then, data exploration was performed using Structured Query Language (SQL), performed on the database with its results organized into tables, graphs and infographics.

The database was enriched by adding 20 new variables, corresponding to the indicators of the WHODAS 2.0 domains with numerical (index from 0.00 to 1.00) and categorical data (class: low <0.33, medium 0.33-0.66 and high >0.66).

To analyze the data from the responses, the likert scale contained in the WHODAS 2.0 instrument was converted into self-assessment indexes ranging from 0.00 to 1.00 using the following equation: question index = (Value in likert scale-1/number of elements in scale-1). We also used the equation for the inversion of negative scales, adopted in the disability domain before applying the geometric mean.

To form the clusters, SimpleK-means was used, defining the formation of two centroids that, based on their majority characteristics, allowed us to label them in groups: Disabled and Enabled.

The rules and association were obtained through the Apriori algorithm, to find dependency relationships among 45 variables: 17 categorical and 28 Boolean (yes/no). For the classification KDD problem, the outcome classes were adopted as the dependent variable. In this task, the Decision Tree (DT) algorithm J.48 trained and tested by the 10-fold cross-validation method was used to create the classification models.

At the end, the models were compared in relation to the characteristics of the input and output variables, their complexity, and quality measures. Based on these models, the variables that most interfere in the outcome of the target attributes were identified.

This work followed the norms of Resolution 466/2012 of the National Health Council with appro-

val number 4,735,765/2021 from the Research Ethics Committee of Plataforma Brasil.

## Results

Of a total of 93 patients eligible for the survey, 35 individuals did not answer the call within three contact attempts, nine died within the first year after discharge, 13 had incorrect or non-existent phone numbers, and four refused to participate in the study.

Thus, 32 individuals (100%) participated in this work, among them 14 (44%) men and 18 women (56%), with a mean age of 57 years. After the data analysis it was possible to gather the individuals into two groups: 8 (25%) individuals fit into the group considered less independent (incapacitated) and 24 (75%) fit into the more independent group (capacitated).

As for functioning in the disabled group, the domains of cognition, mobility, self-care, life activities, and participation were considered low in 4 (50%) of the individuals, and the interpersonal relations domain was represented as low in 3 (37%) of the patients, with 6 (75%) of the individuals having a high level for disability.

The profile of the group of individuals consid-

ered disabled was 2 (25%) men and 6 (75%) women with a mean age of 68 years in the group; 5 (62%) live independently in the community, and 3 (37%) live with assistance, and 4 (50%) are widowed. The clinical profile of the disabled group had 3 (37%) individuals classified as obesity grade I and 3, as obesity grade II (37%) in its predominance with an average of 6 daily use medications among the individuals, 6 (75%) of the interviewees presented some difficulty to sleep and concentration in the last 30 days, 4 (50%) presented some of the depressive symptoms, such as sadness, persistent discouragement and low self-esteem in the last 30 days.

Among the hospitalization factors associated with disability, a mean hospital stay of 27 days was observed, with a mean ICU stay of 12 days. During this period, 7 (87%) patients used antibiotic therapy, 5 (62%) used mechanical ventilation during hospitalization, 6 (75%) had no history of stroke, and 7 (87%) did not require cardiopulmonary resuscitation.

In the Data Mining process, dimensionality reduction was performed by the Correlation-based Feature Selection algorithm, and from the class (low, medium, and high) and unbalanced index of the outcome classes, the variables ( $p < 0.05$ ) with the ability to explain Disability were obtained, as shown in Figure 1.

Attribute Meta	Disability	
	Class	Index
Selected Variable ( $p < 0,05$ )	(100%) - Age (100%) - Had any difficulty sleeping in the last 30 days (100%) - How many medicines do you take per day (97%) - Needed cardiopulmonary resuscitation (97%) - Had mechanical ventilation (97%) - Had difficulty hygienizing/cleaning your mouth in the last 30 days (97%) - Body Mass Index (91%) - Living conditions at the moment of the interview (91%) - Presented any depressive symptoms such as sadness, persistent discouragement and low self-esteem in the last 30 days? (91%) - Brain stroke	(100%) - Living conditions at the moment of the interview (100%) - Needed mechanical ventilation (100%) - Presented difficulty to hygienize/clean his/her mouth in the last days (97%) - Marital status (94%) - How many medicines do you take per day (91%) - Age (91%) - Stroke (88%) - Presented difficulty in concentration in the last 30 days (88%) - Presented some depressive symptom such as sadness, persistent discouragement, and low self-esteem in the last 30 days (81%) - Had some depressive symptom such as sadness, persistent discouragement, and low self-esteem before hospitalization for COVID-19 (72%) - Needed antibiotics

**Figure 1** – Variables with ability to explain Disability after the data mining process. Ponta Grossa, PR, Brazil, 2022

The class is the classification given to the intervals of the index, called categorical data, divided into low ( $\leq 0.33$ ), medium ( $\geq 0.33$  to  $\leq 0.66$ ), or high ( $\geq 0.66$ ) values. The unbalanced index of the outcome classes is a numerical range from 0 to 1, with 1 being optimal. It is evident that variables that appear in both the class and index column are more expressive than others that appear in only a single situation.

Figures 2 and 3 were calculated from the WHODAS 2.0 protocols, adapted for indices. It can be observed that the geometric mean of the Disability indicators presents an index of 0.77. The interpersonal relationships present the highest index among

the indicators, and the disability presents a low index (0.25), which would be ideal, that is, a negative domain, inverse to the capacity.

Through the Mann-Whitney Test, statistical evidence of differences between the means of the groups in all the domains evaluated is presented: Cognition ( $p=0.006$ ), Mobility ( $p<0.000$ ), Self-care ( $p=0.017$ ), Interpersonal relations ( $p=0.011$ ), Activities of life ( $p<0.000$ ), Participation ( $p<0.000$ ), Disability ( $p<0.000$ ). As also occurs between the geometric mean between the groups, observed through the Unpaired t test with Welch correction ( $p=0.000$ ), evidencing that group I presents the worst indicators of Disability.

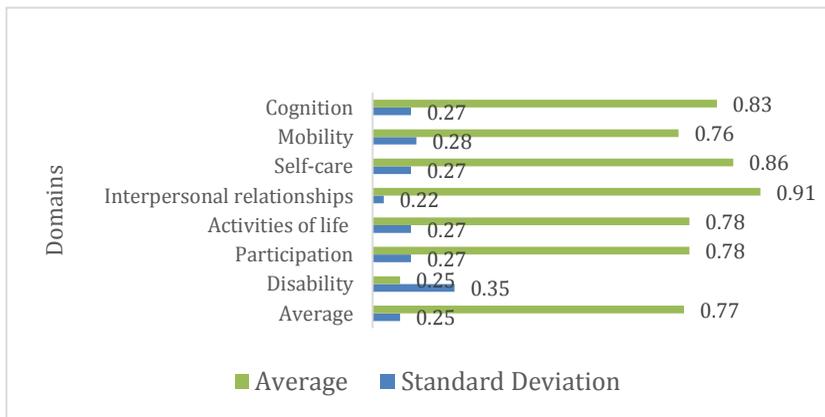


Figure 2 – Disability indicators of the sample. Ponta Grossa, PR, Brazil, 2022 R, Brazil, 2022

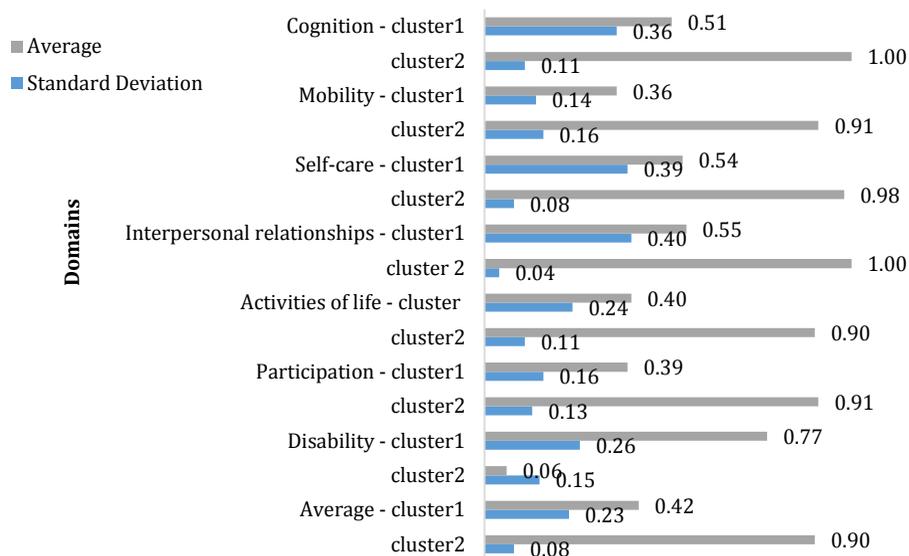
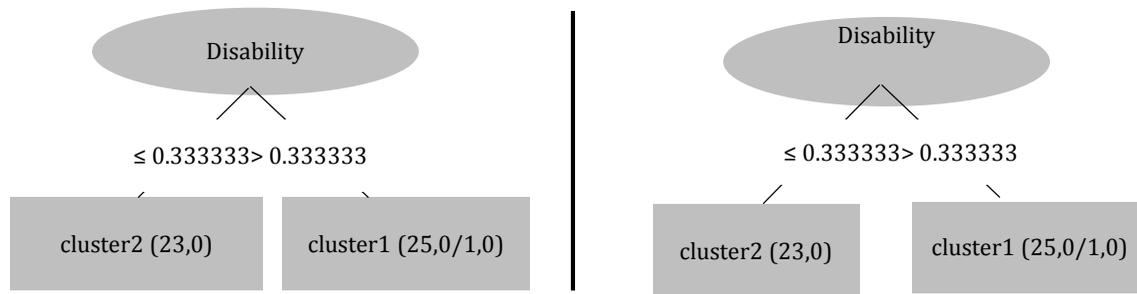


Figure 3 – Disability index by cluster. Ponta Grossa, PR, Brazil, 2022

Figure 4 shows non-complex models with high hit rate and quality measures of the cluster classifications. The initial nodes are the most promising as they

have the highest information gain and lowest entropy. The variable inability is allocated at this location, so it strongly influences the outcome of the decision tree.



**Figure 4** – Decision Tree Models - Infographics. Ponta Grossa, PR, Brazil, 2022

## Discussion

As shown in recent studies, the age group that suffered the highest number of hospitalizations for COVID-19 was those aged over 60 years, being related to the worst prognosis and higher risk of death due to the aging process and the presence of comorbidities<sup>(15-16)</sup>. Regarding the gender of the reported cases, a relatively uniform distribution between women (54.1%) and men (45.9%) is noticed, with variations between age groups<sup>(15)</sup>, considering that 86.9% do not live alone<sup>(17)</sup>.

Thus, the age range over 60 years and the epidemiological changes associated with the increase in chronic noncommunicable diseases such as obesity, hypertension (SAH), and diabetes mellitus (DM) generate the need for pharmacological treatment with several drugs, which leads to the use of four or more drugs, called polypharmacy by experts, which impacts the quality of life of these individuals<sup>(18)</sup>.

As for the presence of comorbidities in these individuals, 41% had hypertension, 29% DM, 37% had grade 1 obesity, 20% grade 2 obesity, 8% grade 3 obesity, and 20% were overweight<sup>(15)</sup>. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) affects pancreatic islet cells, stimulating and altering homeostasis and glucose metabolism, leading to the onset of DM in pre-disposed individuals or worsening the already manifested diabetes<sup>(19)</sup>.

Regarding individuals who present systemic arterial hypertension, these are mostly elderly and sedentary, which may lead to a confusion of data, and studies have reported that SAH itself is not related to COVID-19<sup>(20)</sup>; however, the most severe cases of the disease are correlated with obese individuals, the increased inflammatory response of obesity increases the hyperinflammatory state of the disease, increasing the risk of death and worse prognosis of the disease<sup>(15)</sup>. The mean hospital stay was nine days, and the mean ICU stay was 23 days, with 89.9% and 96.6% of patients receiving antibiotics during hospitalization, hydroxychloroquine and azithromycin, respectively<sup>(21)</sup>.

In this sense, individuals with other critical illnesses who were diagnosed with the severe form of the disease may present cognitive symptoms such as memory loss and altered concentration level, typical of PICS. Concentration and memory deficits may persist for a period of six weeks or more in patients who have been hospitalized due to SARS-CoV-2<sup>(22)</sup>.

Currently, the syndrome is characterized by symptoms that are still considered nonspecific and related to: loss of interest in performing daily activities that were pleasurable before the disease; feeling of low self-esteem; sleep disturbance; and difficulty concentrating. These cognitive symptoms impact the quality of life of patients who have been in the ICU, and the sequelae are proportional to the length of hos-

pitalization with a short- and long-term impact<sup>(23)</sup>.

Thus, it was observed, after hospital discharge, that 259 (28.8%) elderly individuals reported having little interest in performing their life activities; 297 (33.0%) felt depressed, 328 (36.5%) had difficulty sleeping; 134 (14.9%) felt bad about themselves; 228 (25.3%) had difficulty in concentrating<sup>(24)</sup>.

The post-discharge symptoms of 120 patients were evaluated, 34% had memory loss, 28% concentration difficulties and 30.8% sleep disorders<sup>(25)</sup>. It was found that individuals hospitalized for severe disease have long-term persistent symptoms<sup>(26)</sup>, and in six months after hospital discharge, they presented muscle weakness, sleep difficulties, anxiety or depression<sup>(5)</sup>.

Brain Fog, a term used to define the set of neurological symptoms, is characterized by headaches, short-term memory loss and confusion<sup>(27)</sup>. In this sense, patients who required mechanical ventilation are more associated with the appearance of cognitive deficit after infection by SARS-CoV-2 because of the cerebrovascular complications resulting from the disease<sup>(28)</sup>. Problems such as cerebral hemorrhage, stroke and memory impairment are conditions that appear with some frequency in other severe diseases<sup>(29)</sup>.

Respiratory failure secondary to acute respiratory distress syndrome is common in critically ill patients and can lead to cardiac arrest in individuals with coronavirus, and medications that widen the electrocardiogram interval, especially antibiotics (such as Azithromycin and Hydroxychloroquine) are included in some treatment protocols<sup>(30)</sup>.

## Study limitations

As a study limitation, we highlight the fact that this is a cross-sectional study, which hinders the elaboration of greater causal inferences, besides the fact that the sampling technique is non-probabilistic, which prevents excess data.

## Contributions to practice

Certainly, this study contributes to a better understanding of the long-term impacts of COVID-19, providing better treatments and improved quality of life for patients who were affected by SARS-CoV-2 and required hospitalization for long periods in the ICU.

## Conclusion

According to the above, it can be concluded that together, the SARS-CoV-2 virus and factors associated with the days spent in the Intensive Care Unit, the need for mechanical ventilation and the use of antibiotics, added to epidemiological clinical factors such as the presence of comorbidities and age over 60 years, and also added to the difficulty in concentrating and alteration in the sleep pattern after hospital discharge are related to disability in individuals 12 months after discharge from the COVID-19 Intensive Care Unit, impacting the quality of life of these patients.

## Authors' contribution

Conception, design, interpretation of data, relevant critical review of the intellectual content, and final approval of the version to be published: Fadel CB.

Interpretation of the data, drafting of the manuscript, relevant critical review of the intellectual content, and agreement to be responsible for all aspects of the manuscript: Amaral I.

Writing of the manuscript and critical review: Marafigo LRZ, Alves FBT.

Analysis and interpretation of the data: Santos CB.

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