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Original Research

Loneliness, Social Relationships and Family Communication: The Impact on the Mental Health of Severe COVID-19 Survivors in the Long Term

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Abstract

Background: Given the significant physical and psychological impact of coronavirus disease 2019 (COVID-19) in severe survivors, understanding the long-term consequences of psychosocial factors is crucial for developing effective support interventions. **Methods**: The longitudinal impact on emotional distress of loneliness, social relationships, and quality of communication with family members during hospitalization was analyzed in 75 Spain survivors of bilateral pneumonia and respiratory failure who required hospitalization during Wave 1 in a two-year longitudinal study of severe COVID-19. **Results**: The results showed that certain variables at baseline were significant predictors of depressive symptoms two years later: worse perceived health and higher levels of perceived loneliness. Better social relationships and a higher quality of family communication with relatives during the hospitalization significantly predicted lower levels of depression longitudinally. In addition, results showed that being female patient, worse perceived health, and worse social relationships significantly predicted higher levels of anxiety 2 years later. **Conclusions**: Results suggest that psychosocial factors contribute to longitudinally explain distress in patients who have been hospitalized from a severe disease (i.e., COVID-19).

Keywords: severe COVID-19; longitudinal consequences; anxiety; depression; loneliness; family communication; social support

Soledad, Relaciones Sociales y Comunicación Familiar: Estudio Longitudinal del Impacto en la Salud Mental de Supervivientes Graves de COVID-19

Resumen

Introducción: Debido al considerable impacto físico y psicológico que la enfermedad por coronavirus 2019 (COVID-19) ha tenido en los pacientes gravemente afectados, resulta fundamental entender las consecuencias a largo plazo de los factores psicosociales para diseñar intervenciones de apoyo efectivas. **Métodos**: El objetivo de este estudio fue analizar longitudinalmente el impacto de la soledad, las relaciones sociales y la calidad de la comunicación con los familiares durante la hospitalización en el malestar emocional en 75 supervivientes de neumonía bilateral e insuficiencia respiratoria que requirieron hospitalización durante la primera ola de COVID-19 en un estudio longitudinal de dos años. **Resultados**: Los resultados mostraron que ciertas variables en la evaluación inicial fueron predictores significativos de sintomatología depresiva dos años después: una peor percepción de la salud y mayores niveles de soledad percibida. Mejores relaciones sociales y una mayor calidad de la comunicación familiar con los familiares durante la hospitalización predijeron significativamente menores niveles de sintomatología depresiva de manera longitudinal. Además, los resultados mostraron que ser mujer, tener una peor percepción de la salud y peores relaciones sociales predijeron significativamente mayores niveles de ansiedad dos años después. **Conclusiones**: Los resultados sugieren que los factores psicosociales contribuyen a explicar longitudinalmente el malestar en pacientes que han sido hospitalizados por una enfermedad grave (COVID-19).

Palabras Claves: COVID-19 severo; consecuencias longitudinales; ansiedad; depresión; soledad; comunicación familiar; apoyo social

1. Introduction

Coronavirus disease 2019 (COVID-19) can be considered as a situation of acute stress, especially for people who were affected in wave 1, as they required hospitalization, and had to cope with a very demanding and unpredictable situation (e.g., lack of communication with their family members at hospital; Whitehead and Torossian, 2021). Given the nature of this dramatic situation it is not surprising that different studies have shown important negative consequences for the physical and emotional health (e.g., depression) of the people affected by it (e.g., Huang et al, 2021). In order to analyze the inherent impact of situations of natural disasters and pandemics, results of previous studies suggest that the variability between the different reactions to the pandemic found in the population depend on factors such as perceived health, previous mental health, level of social support, coping strategies and socioeconomic context, among others (Cedeño et al, 2020). The difficulty of having family visits at the hospitals, and the uncertainty of knowing the evolution and impact of COVID-19 on patients and their relatives, may have led to feelings social isolation and loneliness, variables strongly associated with negative consequences for mental health (e.g., depression; Jurblum et al, 2020).

However, most of the existing literature about the impact of COVID-19 on mental health has been conducted with non-hospitalized patients and using cross-sectional study designs. In the scarce number of existing longitudinal studies about COVID-19, most of them have focused on analyzing the prevalence rates of emotional symptoms (e.g., Cénat et al, 2022; Houben-Wilke et al, 2022), with studies showing that 26% of hospital survivors with COVID-19 reported anxiety or depressive symptoms one year later (Huang et al, 2021), although information about predictors of this distress remains scarce. A recent systematic review, conducted in long COVID patients or with persistent symptoms after 4 weeks from recovery, suggested that the most common emotional symptoms found in these patients were depression, posttraumatic stress and, specially, anxiety (Marchi et al, 2023). Although evidence suggests, about depression and anxiety, to be a co-occurring phenomenon and predictive factors of long COVID (Engelmann et al, 2024), the exploration of predictors of these long-term impacts, particularly in hospitalized populations, remains underdeveloped. Moreover, understanding the role of modifiable factors, such as family communication during hospitalization, perceived social support and loneliness, which are well-known risk factors of emotional distress in other populations (Wang et al, 2018), could allow researchers to developed targeted interventions for at-risk hospitalized populations.

Among the existing studies on risk factors associated with suffering a high psychological impact derived from the pandemic, a few stand out: being female, younger, having a low educational level, the existence of previous psychological disorders, loneliness, negative perception of one's own health, living alone and working in healthcare (Broche-Pérez et al, 2021; Cortés Zamora et al, 2022; MacDonald et al, 2022). Another factor that frequently modulates the psychological impact of stressful situations, such as the COVID-19 pandemic, on emotional distress (e.g., anxiety) is social connections and support (Xu et al, 2020). However, the longitudinal role of predictors of emotional distress in hospital survivors who suffered from severe COVID-19 in Wave 1 have been scarcely studied. Within the general population, studies have highlighted the importance of social support (Jónsdóttir et al, 2025), as well as psychological variables such as psychological flexibility (Sebastião and Neto, 2025), in predicting better long-term mental health outcomes. Among the limited longitudinal studies conducted with survivors of severe COVID-19, the use of invasive mechanical ventilation has been identified as a significant predictor of both depression and post-traumatic stress symptoms (Navarra-Ventura et al, 2024). Yet, no studies to date have specifically focused on analyzing psychosocial predictors of emotional distress in this high-risk population. Exploring these predictors on severe patients hospitalized during the COVID-19 pandemic, may be of several importance, not only for those who still experience the consequences of the pandemic (i.e., long COVID, or COVID survivors who still experiences emotional consequences of the disease process), but for other kinds of hospitalized patients with similar conditions of uncertainty. Loneliness and lack of social support are common problems in various patient groups, such as those in intensive care units' patients, or with complex chronic illnesses, who often required hospitalizations (e.g., Christiansen et al, 2021). By exploring the longitudinal relationships between these uncovering risk and protective factors and mental health outcomes, research may contribute to a better understanding of the psychosocial support needs of vulnerable populations during and after hospitalization. Identifying these modifiable key factors enables the creation of prevention initiatives (e.g., fostering family communication during hospitalization) or interventions that could prevent long-term emotional distress and improve the quality of life of different types of patients.

Therefore, this study aimed to analyze the role of quality of family communication during hospitalization, perceived loneliness and social relationships on emotional distress (depression and anxiety symptoms) in survivors of bilateral pneumonia and respiratory failure in Wave 1 of COVID-19 in a two-year longitudinal study. We hypothesized that lower loneliness, having higher quality of family communication during hospitalization and presenting better social relationships would predict lower emotional distress.

2. Method

2.1 Participants

Participants consisted of 75 adult survivors of severe COVID-19 of Wave 1 of the pandemic. The number of participants two years after baseline was 68. Baseline assessments were conducted in October 2020 and the follow up assessments were conducted two years after baseline.

Participants were recruited from different hospital and health centers from the Community of Madrid (Spain). We contacted two health institutions in the Community of Madrid: Severo Ochoa Hospital and the Salesas Health Center. Both centers agreed to participate in the study. A physician (Internal Medicine Specialist) at Severo Ochoa Hospital and a nurse at the Salesas Health Center explained the purpose of the study to participants. They then provided us with a list of patients who met the inclusion criteria and who had expressed interest in participating. Following this, individual telephone interviews were conducted by a psychologist trained in the assessment protocol. Inclusion criteria were to have been a patient with severe COVID-19 in Wave 1 (between March 2020 and June 2020), had been diagnosed with bilateral pneumonia and respiratory failure, required hospitalization due to these conditions during Wave 1 and being 18 years old or older. Exclusion criteria were to have been a patient of COVID-19 without severe symptoms (bilateral pneumonia and respiratory failure) and/or to present cognitive or psychiatric dysfunctions that may interfere in understanding the aims of the study. Baseline characteristics of the sample are shown in Table 1. Most of participants were male (73.3%), with an average age around 60 and almost half of them were retired (48.6%). The average time of hospitalization was 18.60 days.

2.2 Instruments

Sociodemographic variables. Information on the following sociodemographic and contextual variables was collected: gender (0 = male; 1 = female), age, perceived health (with a single item, "in this moment, how do you consider your health", with scores ranging between 1 = very bad, 2 = quite bad, 3 = quite good, and 4 = very good).

In addition, the following variables were evaluated:

Social relational variables:

Quality of family communication. Family communication with relatives during the hospitalization for COVID-19 were assessed with dichotomic options (yes/no) for three different forms of communication: via telephone, videocall or face to face. Then, the "communication levels" variable was created according to the following codification: 0 = only telephone communication was conducted (nor videocall nor face to face communication), 1 = videocall communication (even when also they have telephone call communication) and 2 = face to face communication (even when also they could have communication through the telephone with call or videocall). We consider that higher scores in this variable are indicative of higher quality of family communication. There were four participants who had no communication at all, so they were removed from the group.

Social relationships. Social relationships were assessed after hospitalization, using an item of the Spanish version of the Gijon social-family scale (Alarcón-Alarcón and González-Montalvo, 1998), (with answers ranging 1 = several relationships, 2 = with family members and neighbors, 3 = with family members or neighbors, 4 = did not leave the home but had visits, 5 = did not leave the home or have visits).

Loneliness. Perceived loneliness was measured using one item ("how lonely do you feel in this moment?"), with answers ranging from 0 (not at all) to 10 (absolutely).

Emotional outcomes:

Depression and anxiety symptoms. Depression and anxiety symptoms were measured using the Spanish version of the Hospital Anxiety and Depression Scale (HADS) by Tejero (2003). Each subscale consists of 7 items assessing depressive and anxiety symptoms during the previous week, with scores ranging from 0 (not at all) to 3 (very often). Scores lower than 7 are indicative of normal symptoms, scores between 8 to 10 indicate likelihood of symptoms of depression/anxiety and scores equal to or above 11 usually identify people with clinical depression/anxiety. Cronbach Alpha of this scale in this study was 0.70. The Spanish version of the HADS shows good validity indices, including high discriminative capacity with Area Under the Curve (AUC) values of 0.92 for anxiety and 0.88 for depression, and adequate sensitivity/specificity levels (80%/85% for anxiety; 72%/87% for depression; Herrero et al, 2003).

2.3 Procedure

Physicians and health collaborators contacted the participants in their post-COVID-19 check-up consultations, who then informed the participants about the aims of this study and made sure they met the inclusion criteria. Patients who wanted to participate in the study signed the informed consent at the hospital. For those patients whose clinical or/and functional situation did not allow them to attend to the hospital, the aims of the study were explained via telephone. After that, individual telephone interviews to assess the variables of the study were conducted by trained psychologists during a two-year period, with one individual interview at baseline and a second interview after two years (2-year follow up assessment). Participants were contacted by telephone for follow-up assessments, which were conducted via phone. Participants were considered lost to follow-up if they did not respond or reschedule their assessment appointment at least four times. No financial compensation was provided for study participation.

The study protocol was approved by the Ethics Committee of the Hospital Universitario Severo Ochoa.

Table 1. Descriptive characteristics of the sample at baseline.

	M	SD	Range	%	N
Gender					75
Male				73.3	55
Female				26.7	20
Age (years)	60.09	12.78	30–80		
Work Status					72
Employed				51.4	37
Retired				48.6	35
Monthly income	1661.85	886.09	500–5000		
Days at hospital	18.60	23.45	1–128		
Number of family members with COVID-19	2.15	2.63	0–15		
Perceived health					75
Very bad				10.7	8
Bad				41.3	31
Normal				24.0	18
Good				22.7	18
Very Good				1.3	1
Social Relationships	1.52	0.86	1–4		75
Relationships (several)				69.3	52
With family members and neighbors				12.0	9
With family members or neighbors				16.0	12
Does not go out but has visits				2.7	2
Does not go out nor has visits				0.0	0
Communication with relatives					71
Telephone				23.9	17
Videocall				70.4	50
Face-to-face				5.6	4
Current loneliness	2.27	2.60	0–10		
Depressive symptoms	9.53	2.93	4–16		
Anxiety symptoms	8.52	4.36	2–19		

COVID-19, coronavirus disease 2019; N, number of patients; M, mean; SD, standard deviation.

2.4 Data Analysis

Firstly, univariate and multivariate outliers and normality were assessed. In addition, descriptive analyses were conducted to analyze the characteristics of the sample (means, standard deviations and range). To analyze the effects of quality of family communication, social relationships and perceived loneliness on the patients emotional outcomes, two regression analyses, for depression and anxiety symptoms respectively, were carried out after controlling for baseline levels of emotional distress and sociodemographic variables. As a first step, baseline levels of emotional distress (depression and anxiety symptoms) were introduced in each of the regression models. In the second step, gender, age, perceived health, loneliness, social relationships and family communication, were included in the models. The amount of explained variance was calculated for each model. All analyses were conducted using SPSS Software (version 27.0, IBM Corp., Chicago, IL, USA).

3. Results

3.1 Outliers and Normality

Skewness and kurtosis were within the expected values. Neither univariate nor multivariate outliers (Mahalanobis distance at $p < 0.001$) were found.

3.2 Predictors of Longitudinal Emotional Distress

Regarding depressive symptoms, results presented in Table 2 show that the proposed model explained 35.2% of depressive symptoms 2 years after COVID-19. Specifically results show that patients who reported worse perceived health and higher levels of loneliness presented higher levels of depressive symptoms two years later. In addition, a higher number of social relationships and a higher level of quality of family communication were associated with lower levels of depressive symptoms two years later. No significant effects on depressive symptoms were found for baseline depressive symptoms, gender or age.

Regarding anxiety symptoms, results show that the proposed model explained 32.7% of anxiety symptoms after COVID-19 (see Table 2). Results show that survivors who reported worse perceived health and social relation-

Table 2. Results of the hierarchical regression models for depression and anxiety symptoms at two years follow up.

	Step	Predictor	β	t	ΔR^2
Depression	1	Depression at baseline	0.05	0.42	0.003
	2	Depression at baseline	–0.04	–0.33	0.349
		Gender	0.09	0.75	
		Age	0.19	1.67	
		Perceived health	–0.25	–2.19*	
		Perceived loneliness	0.46	3.62**	
		Social relationships	–0.33	–2.62*	
		Family communication	–0.24	–2.20*	
Anxiety	1	Anxiety at baseline	–0.14	–1.14	0.002
	2	Anxiety at baseline	–0.21	–1.81	0.325
		Gender	0.26	2.25*	
		Age	–0.22	–1.95	
		Perceived health	–0.32	–2.78**	
		Perceived loneliness	0.25	1.96	
		Social relationships	–0.26	–2.09*	
		Family communication	–0.09	–0.74	

Note. *$p < 0.05$; **$p < 0.01$.

ships presented more anxiety symptoms two years after COVID-19. In addition, female patients presented higher levels of anxiety symptoms 2 years later. No significant effects were found on anxiety symptoms for baseline anxiety symptomatology, age and loneliness.

4. Discussion

The aim of this study was to analyze longitudinally if psychosocial variables (loneliness, social relationships, and quality of family communication during hospitalization) were associated with emotional distress (depression and anxiety symptoms) in patients of severe COVID-19 in the first Wave 1 of pandemic, two years after being hospitalized, after controlling for gender, age, perceived health as well as for emotional symptoms at baseline. This study adds to previous literature, mostly focused on analyzing the physical and psychological impact of the COVID-19 pandemic cross-sectionally (Cortés Zamora et al, 2022; Huang et al, 2021), we have aimed to increase the knowledge regarding potential psychosocial predictors of emotional health outcomes longitudinally in survivors of severe COVID-19 in Wave 1. To our knowledge no studies have focused on the role of risk factors on emotional health in hospitalized patients with severe COVID-19 two years after being hospitalized, being, at this moment, only one study available that has a one year follow up (Cortés Zamora et al, 2022; Méndez et al, 2022). Specifically, results of our study suggest that higher levels of loneliness and a lower number of social relationships predict higher levels of depressive symptoms two years after being hospitalized, which is consistent with previous cross-sectional studies (e.g., Meyer et al, 2020) and longitudinal studies in non-hospitalized population (e.g., MacDonald et al, 2022), as loneliness and social support are well-documented risk factors for depression across diverse populations and contexts (Cacioppo et al, 2006). Results also suggest that, in the context of COVID-19, the prolonged social restrictions and high level of physical limitations, either during and after hospitalization, may likely exacerbate feelings of loneliness, which may increase vulnerability to develop depression two years later. Prolonged isolation during hospitalization for COVID-19 survivors, coupled with the challenges of re-establishing social connections post-discharge, likely amplifies emotional vulnerability. Our findings highlighted the need for comprehensive psychosocial assessments as part of post-hospitalization care, particularly for those recovering from severe illnesses like COVID-19, specially addressing loneliness and social support during critical transitions from hospital to home. Assessing and designing strategies targeting loneliness and social support may be useful for enhancing long-term emotional distress in patients recovering from severe illnesses.

In addition, patients who had worse quality of communication with their relatives (measured as lower levels of family communication) while being hospitalized presented higher levels of depression longitudinally, which suggests that a better quality in family communication may play a relevant role in explaining emotional discomfort, having practical suggestions for the humanization of care. These results are consistent with studies in other populations that highlight the relevant role that social support and family communication variables have on explaining depression (Curran and Allen, 2017). These results suggest that encouraging a better quality of family communication during hospitalization (e.g., face to face) may be a modifiable and a key target in preventing depression symptoms, an outcome which has been associated longitudinally with poor functional recovery in hospitalized COVID-19 survivors (Lorent et al, 2022). The inclusion of family cohesion as a protective factor to buffer effects of stress and to explain

health outcomes has been previously addressed (Fosco et al, 2023; Montirosso et al, 2021). Although previous studies have examined the effects of the type of communication (e.g., digital communication such as the use of social media) when face-to-face interaction was limited in the first wave of COVID-19 (e.g., Nguyen et al, 2022), as well as the impact of the type of communication in physician-patient interactions (Hammersley et al, 2019), until now, no study had explored how the mode of communication between a hospitalized patient and his relatives during admission for a severe contagious illness, relates to adverse emotional outcomes such as long-term depression two years later. Results of this study suggest that patients who were able to maintain better communication with family members during hospitalization exhibited significantly lower levels of anxiety and depression two years later. These results suggest that fostering effective family communication during critical care not only humanizes the healthcare process but also may serve as a preventive measure against future emotional distress.

Also, our results suggest that reporting a worse perceived health longitudinally predicts a higher level of depressive symptoms which is consistent with other studies (Sullivan et al, 2017). This finding has potential clinical implications, as previous studies have shown that depressive symptoms are associated with hospital readmissions (Cancino et al, 2014), and targeting psychological correlates of depression such as encouraging family communication at hospitals and social support may reduce perceived loneliness in patients, which could prevent clinically depressive symptoms over time.

Regarding anxiety symptoms, results of this study show that worse perceived health and low social support significantly predicted higher levels of anxiety symptoms 2 years after being hospitalized. In this line, it has been found that higher emotional support from healthcare workers during hospitalization is a protective factor for posttraumatic stress symptoms one-month post-discharge in COVID-19 survivors (Ju et al, 2021).

In addition, results of this study suggest that being a female survivor patient significantly predict anxiety symptoms in long term, which is consistent with previous literature, as women may often being exposed to more caregiving roles, influenced by societal and cultural expectations (Matud and García, 2019). It is important to acknowledge that the small sample size of female participants constitute a limitation of the study. It would be interesting to analyze gender differences in the associations between psychosocial variables and emotional health in future studies to identify the specific needs of people of different genders. Previous studies highlighted the important role of social support on the association between gender and emotional outcomes (Swickert and Hittner, 2009), suggesting that emotional social support predict psychological distress specially in women (Matud and García, 2019). The design of future studies with gender stratification is recommended.

This study presents some limitations. First, the small sample size of the study limits the generalizability of the conclusions, although this is the first exploratory study that analyzes predictors of longitudinal emotional consequences in a specific profile of participants, patients with severe COVID-19 disease who were hospitalization during Wave 1 of the pandemic. Future studies with larger samples and a priori power analyses would be crucial to confirm and extend our preliminary findings. Due to the pilot nature and time constraints of this longitudinal study with post-pandemic survivors, telephone interviews were conducted using self-reported measures with ad hoc items to measure some key variables (e.g., quality of family communication and perceived loneliness), rather than established, validated scales, which constitute an important limitation of this study. Consequently, it was not possible to report the psychometric properties of these variables, which represents an additional limitation. This could potentially compromise the generalizability and reliability of our findings. Future research should prioritize the development and utilization of well-validated, comprehensive scales to quantify these constructs accurately, particularly considering both frequency of and quality of family communication during hospitalization (e.g., Wongpakaran et al, 2020). Although this is a longitudinal study, this does not allow us to infer causal relationships between the variables of the study. In addition, future research should consider also the differences between those patients reporting any of these kinds of family communication and those who did not having any kind of communication at all during their hospital stay. These analyses were not possible to be considered for the present study, due to the small number (n = 4, 5.9% of the total sample) of participants who did not report any kind of family communication during their stay. Therefore, future studies with larger sample sizes should try analyzing these different groups, in order to stablish clearer associations between family communication and psychological well-being in hospitalized patients. Moreover, an important limitation of the present study is the absence of objective measures of the participants' physical health status, as well as the lack of information regarding any psychological or psychiatric treatment received during the two years following hospitalization. These variables could have significantly contributed to explaining the current emotional distress and should therefore be considered in future longitudinal studies. Finally, another limitation of this study is the absence of intermediate assessments (e.g., a one-year follow-up) between baseline and the two-year follow-up. The two-point assessment design may have missed potential fluctuations or changes in the variables of interest over time. Future studies would benefit from incorporating multiple time points to better understand the trajectories and dynamics of emotional distress in patients following hospitalization. Given the mentioned limitations, it is important to be cautious when generalizing the conclusions of this

study. In spite of these limitations, this study adds to previous longitudinal studies in hospitalized patients with severe COVID, which found negative consequences of COVID-19 for depression and anxiety symptoms (e.g., Huang et al, 2021). We highlight the important role of psychosocial predictors (loneliness, social support and quality of family communication during hospitalization) on these outcomes.

5. Conclusions

Although our conclusions may not be directly applicable to the current situation of the COVID-19 pandemic, since it has ended, we consider that our preliminary findings, highlighting the potential significant role of social factors and family communication in explaining emotional distress over time, may have implications for understanding and addressing the needs of patients with symptom persistent COVID-19 or other populations who have experienced critical illness, such as intensive care unit (ICU) survivors. These individuals may often face similar challenges related to physical and psychological recovery, and our research suggests that high social support, low perceived loneliness and an effective family communication during hospitalizations could play a crucial role in their well-being.

Therefore, this study may present important clinical implications for the humanization of care. First, preliminary results suggest that perceived loneliness and presenting better quality of communication with relatives during hospitalization, which is a very critical and uncertain situation, may contribute to longitudinally explain consequences on emotional distress. It would be useful to foster and promote communication with family members and social connections as key components during critical care and hospitalization processes, as this may prevent the development of future emotional distress problems in patients. These results may be applied to other clinical populations (e.g. intensive care units or complex chronic diseases) which have important clinical implications for social and public health systems.

The preliminary findings obtained in this study may contribute to understanding the long-term emotional impact on patients hospitalized for severe COVID-19, as well as clinical implications to identify populations at risk in which it would be important to implement prevention strategies and treatments from a multidisciplinary approach. To continue studying the long-term emotional, physical, and comorbid consequences and their predictors in these patients, in order to provide them with the necessary psychological support, should be greatly encouraged.

Availability of Data and Materials

The authors had full control of all the primary data and the datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

RRM designed and supervised the study, performed the analyses, and wrote the first draft of the manuscript. YCV and PVL collected the data, provided resources, and contributed to manuscript revision. CVG contributed to study design, methodology, and manuscript writing. LMG and MCMA collected data and contributed to manuscript revision. MAF and AVC contributed to methodology, formal analysis, and manuscript revision. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki, and the study protocol was approved by the Ethics Committee of the Hospital Universitario Severo Ochoa (approval number: 0820). All participants gave their informed consent for inclusion before they participated in the study.

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Conflict of Interest

The authors declare no conflict of interest.

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