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Cogitare Enfermagem

REVIEW

COGNITIVE AND FUNCTIONAL CHANGES FOUND IN POST-COVID-19 SYNDROME IN ELDERLY PEOPLE: INTEGRATIVE REVIEW

HIGHLIGHTS

1. The literature presents a wide variety of post-COVID-19 symptoms.
2. High prevalence of sleep disorders, memory, attention, and fatigue.
3. Less persistence of symptoms in men.
4. Clearer definitions of diagnostic criteria and management are needed.

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ABSTRACT

Objective: To identify the most frequent cognitive and functional changes in elderly people after the acute phase of COVID-19. **Method**: Integrative literature review with a search for articles in the LILACS, MEDLINE, PubMed, and Scopus databases, between June and July 2024. The selection was conducted independently by two reviewers and validated by a third reviewer. Original primary studies were included that involved participants with a majority or median age over 60 years, with post-COVID-19 cognitive and functional changes. **Results**: Heterogeneity was observed in the samples, with a wide range of clinical characteristics, the most prevalent being: dyspnea, fatigue, changes in sleep patterns, and cognitive deficit. **Conclusion**: The results contribute to a better assessment and conduct. They point to the need to create specific care protocols for elderly people with post-COVID-19 syndrome and to develop more appropriate and targeted interventions for the prevention, reduction, or minimization of persistent symptoms.

KEYWORDS: Post-acute COVID-19 syndrome; Long COVID; Aged; Review.

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INTRODUCTION

The COVID-19 pandemic, caused by the SARS-CoV-2 virus, has had a significant global impact. By mid-July 2023, more than 767 million confirmed cases and more than six million deaths had been reported worldwide[1]. This disease was classified as a Public Health Emergency of International Concern (PHEIC) from January 30, 2020, to May 5, 2023, as declared by the World Health Organization (WHO)[2].

Despite the downward trend in mortality rates, hospitalizations, and admissions to Intensive Care Units (ICU) due to COVID-19, the WHO recommends formulating long-term strategies to tackle the disease[2]. The high transmissibility of the virus remains a significant challenge, with relevant repercussions on public health, society, and the global economy[3-4].

Infection with SARS-CoV-2 can result in a variety of symptoms and clinical consequences. About half of the infected people may develop post-acute sequelae, known as Post-Acute COVID-19 Syndrome (PACS) or long COVID-19, presenting persistent symptoms that can last for months[5-6]. The WHO established the code RA02 for long COVID-19 in the International Classification of Diseases, version 11[1].

PACS manifests itself through various symptoms, such as chronic fatigue, headache, neurocognitive changes, depression, irritability, insomnia, cardiac and dermatological disorders, and changes in skeletal muscle. These symptoms can hinder the accurate assessment of the syndrome and its prevalence in the population[7-11].

In the case of elderly people infected with SARS-CoV-2, advanced age emerges as a predominant risk factor for the severity and morbidity of the disease. Immunosenescence, an inherent characteristic of aging, makes these individuals more susceptible to serious complications arising from COVID-19[12]. Some recent studies[13-14] have shown that more than a quarter of elderly people developed new conditions after COVID-19 infection, including frailty, increased propensity to sarcopenia, and lower physical performance, when compared to adult individuals.

PACS in elderly people presents a heterogeneous clinical spectrum, manifesting through various symptoms, such as cognitive impairment, delirium, and deterioration of the general state, which makes its identification difficult[11]. Furthermore, pre-existing comorbidities in these individuals may exacerbate the infection, resulting in unfavorable outcomes due to the pathophysiological changes associated with aging[15-16].

In light of these considerations, the purpose of this study was to identify the most frequent cognitive and functional changes in elderly people after the acute phase of COVID-19. The study aimed to analyze the prevalence and symptomatology associated with PACS, as well as to identify possible risk factors that impact the quality of life and functional capacity of these individuals.

METHOD

This is an integrative literature review[17-18], conducted based on six methodological steps, as described below: 1) identification of the theme and selection of the guiding question; 2) establishment of criteria for inclusion and exclusion of studies; 3) definition of

the information to be extracted from the selected studies and categorization of these; 4) methodological evaluation of the included studies; 5) interpretation of the results; and 6) presentation of the review and synthesis of knowledge[19].

For the formulation of the guiding question, the PICo strategy was adopted, where "P" represents the study population (elderly individuals), "I" refers to the phenomenon of interest (cognitive and functional changes), and "Co" denotes the context (PACS).

In the initial stage of the research, the following guiding question was developed: what are the cognitive and functional changes in PACS in elderly people?

Between June and July 2024, a search was conducted in scientific databases, including the Virtual Health Library (BVS), the Medical Literature Analysis and Retrieval System Online (MEDLINE), U.S. National Library of Medicine (PubMed), and Latin American and Caribbean Literature in Health Sciences (LILACS). The Scopus database was also consulted, which has restricted access, being accessed for free through credentials provided to students by the Universidade Católica de Brasília (UCB).

For the article search, keywords and indexed terms in the Health Sciences Descriptors (DeCS) and *Medical Subject Headings* (MeSH) were used: *post-acute covid-19 syndrome, long covid-19, long covid-19 syndrome, persistent covid-19 symptoms, aged, older adults, signs and symptoms* and *complications*.

The eligibility criteria were established, which include primary original articles, such as cross-sectional, cohort, and case-control studies, published in Portuguese, English, or Spanish. There was no restriction regarding the study design or the time of publication. Studies involving participants aged 50 years or older were also included, with a median age of over 60 years.

Articles that did not address the proposed topic, those that did not present a definition of the participants' age range, as well as those that included subjects under 50 years old, were excluded. In addition, studies that were repeated in databases, publications whose results had not yet been disclosed, reviews, letters to the editor, experience reports, and clinical cases were excluded.

The intersection of these descriptors was performed using the boolean operators *AND* and *OR*, as shown in Table 1.

Table 1 - Databases consulted for the composition of the sample in the study. Brasília, DF, Brazil, 2024

	Search strategy used for conducting the research – combination of keywords
MEDLINE	*("post-acute covid-19 syndrome" OR "long covid-19" OR "long covid-19 syndrome" OR "persistent covid-19 symptoms") AND ("aged" OR "older adults") AND ("signs and symptoms" OR "complications")*
SCOPUS	*TITLE-ABS-KEY ("post-acute covid-19 syndrome" OR "long covid-19" OR " long covid-19 syndrome" OR "persistent covid-19 symptoms") AND ("aged" OR "older adults") AND ("signs and symptoms" OR "complications")*

PUBMED	*(("post-acute covid-19 syndrome" OR "long covid-19" OR "long covid-19 syndrome" OR "persistent covid-19 symptoms") AND ("aged" OR "older adults")) AND ("signs and symptoms" OR "complications")*
LILACS	*("post-acute covid-19 syndrome" OR "long covid-19" OR "long covid-19 syndrome" OR "persistent covid-19 symptoms") AND ("aged" OR "older adults") AND ("signs and symptoms" OR "complications")*

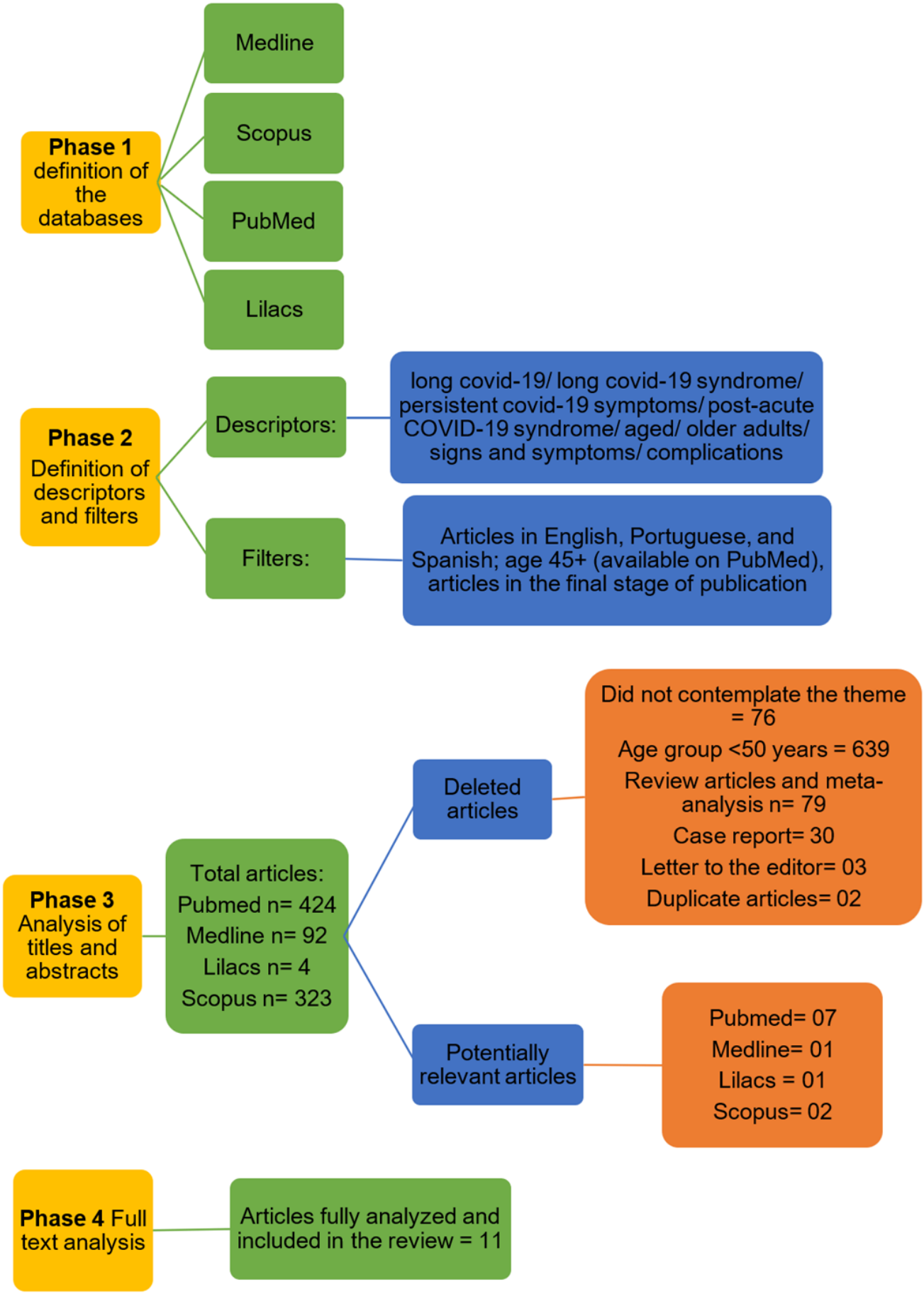
Source: Authors (2024).

This integrative review was registered in the *Center of Open Science registered* (OSF) system, with the registration protocol DOI:10.17605/OSF.IO/GFC8M, and can be accessed through the link: https://osf.io/gfc8m/.

To minimize the risk of bias, the following measures were adopted: (i) the selection of studies was conducted independently by two researchers, with a third researcher consulted to resolve any discrepancies, ensuring impartiality in the inclusion of studies; (ii) eligibility criteria were established to ensure the relevance and quality of the selected articles, including a clear definition of the participants' age range and the exclusion of duplicate studies or those with incomplete data; (iii) data extraction was standardized and meticulously documented, ensuring consistency and accuracy of the collected information.

The instruments were used for the methodological evaluation of the studies, **allowing the identification of potential sources of bias,** such as the lack of blinding or inadequate control of confounding factors. The stages of article selection are presented in Figure 1.

Figure 1 - Flowchart of the search process, selection stages, and reasons for exclusion of studies selected for the integrative review. Brasília, DF, Brazil, 2024



Source: Authors (2024).

RESULTS

11 articles that met the previously established selection criteria, identified in Table 2, were analyzed. The type of study, objective, instruments, and results are summarized in Table 3.

Table 2 – Identification of articles included in the integrative review. Brasília, DF, Brazil, 2024

Identification	Article title	Country and year of publication	Periodical	Sample
A1[20]	*Symptoms after COVID-19 vaccination in patients with persistent symptoms after acute infection: a case series*	United Kingdom, 2021	*Annals of Internal Medicine*	36 patients, average age of 64 years
A2[21]	*Number of initial symptoms is more related to long COVID-19 than acute severity of infection: a prospective cohort of hospitalized patients.*	France, 2022	*International Journal of Infectious Diseases.*	316 patients, mean age of 64.1 years, 59% men
A3[22]	*Neuropsychological measures of long COVID-19 fog in older subjects*	Italia, 2022	*Clinics in Geriatric Medicine*	100 people, average age of 73.4 years
A4[23]	*6- and 12-month outcomes in patients following COVID-19-related hospitalization: a prospective monocentric study.*	Italia, 2022	*Internal and Emergency Medicine*	64 people, average age of 68 years, 64% men
A5[24]	*Post-infection cognitive impairments in a cohort of elderly patients with COVID-19.*	China, 2021	*Molecular Neurodegeneration.*	1,539 patients, age over 60 years, 466 controls.
A6[25]	*Long COVID and chronic fatigue syndrome: a survey of elderly female survivors in Egypt.*	Egypt, 2021	*International Journal of Clinical Practice*	115 women, aged 60 and over.
A7[26]	*Respiratory and psychophysical sequelae among patients with covid-19 four months after hospital discharge*	Italia, 2021	*Jama Network Open*	238 people, aged between 50 and 71 years
A8[27]	Sociodemographic and clinical characterization of elderly people with COVID-19 sequelae.	Brazil, 2023	Revista de Enfermagem UERJ	204 medical records of elderly people (with records of COVID-19 sequelae).

A9[28]	*Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study*	United States, 2022	BMJ	87,337 people aged 65 or older.
A10[29]	*Hand grip strength before and after SARS-CoV-2 infection in community-dwelling older adults.*	Ecuador, 2021	*Journal of the American Geriatrics Society*	254 people with an average age of 70.7 years
A11[30]	*General and orofacial symptoms associated with acute and long COVID-19 in 80 – and 90 – year-old Swedish COVID-19 survivors.*	Sweden, 2024	*Journal of dentistry*	People aged 80 and people aged 90 in the year 2022

Source: Authors (2024).

Table 3 - Presentation of the synthesis of the articles included in the integrative review. Brasília, DF, Brazil, 2024

	Type of study	Objective	Instruments	Results
A1[20]	Observational, prospective - case series.	Describe the quality of life and symptoms after vaccination against SARS-Cov-2 in a series of patients with post-COVID-19 symptoms over eight months.	SF-36, WEMWBS, standardized symptom review.	**Frequent:** fatigue 75%, dyspnea 61%, insomnia 53%. Observations: there was no significant worsening in quality of life metrics before *versus* after vaccination.
A2[21]	Prospective cohort.	Evaluate the risk factors associated with long COVID-19.	Clinical examination, blood count, tomography, symptom questionnaire.	**Frequent:** dyspnea 39.2%, asthenia 37.1%, difficulty concentrating 10.1%, anxiety 9.2%, anosmia 6.3%, alopecia 6.3%, cough 6%, myalgia 5.1%, ageusia 4.7%, chest pain 4.4%, headache 2.2%. Observations: female gender, hypertension, and a high number of initial symptoms related to increased risk of long COVID-19.

A3 [22]	Prospective cohort.	Investigate post-COVID-19 neurological and cognitive characteristics.	Mini Mental State Examination; Rey Auditory Verbal Test; *Multiple Features Target Cancellation; Trial Making Test; Digit Span Forward and Backward*; Frontal Assessment Battery; Hamilton anxiety and depression scales; Psychological distress scales *Kessler; Pittsburg Sleep Quality Index*	**Frequent:** fatigue 49%, sleep disorders 33%, attention impairment 30%, memory impairment 30%, myalgia 17%. Observations: men showed less persistence of post-COVID-19 symptoms and less impact on quality of life scores.
A4[23]	Prospective cohort.	Investigate the long-term symptoms post-severe COVID-19.	Clinical evaluation, interview, laboratory tests, pulmonary function test, computed tomography, and six-minute walk test. Zung's Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS).	**Frequent at six months:** anxiety 48.5%, depression 56.3%, dyspnea 36%, abnormal tomographic findings 80.7%. **Frequent at 12 months:** anxiety 50%, depression 61%, dyspnea 18.7%, abnormal tomographic findings 63.8%.
A5 [24]	Prospective cohort.	Evaluate cognitive status and longitudinal cognitive decline.	*Telephone Interview of Cognitive Status 40* (TICS-40), *Informant Questionnaire on Cognitive Decline in the Elderly* (IQCODE).	**Frequent:** Severe COVID-19: 29.24% with cognitive decline. Non-severe COVID-19: 28.67% with cognitive decline. Control group: 21.46% with cognitive decline.
A6[25]	Retrospective cohort.	Investigate the presence of post-COVID-19 symptoms as a risk factor for Chronic Fatigue Syndrome.	Mixed electronic questionnaire.	**Frequent:** fatigue 57.4%, musculoskeletal symptoms 48.6%, sleep disorders 63.47%, respiratory symptoms 41.73%.
A7[26]	Prospective cohort.	Check for respiratory, functional, and psychological sequelae post-COVID-19.	*Pulmonary Function Test (PFT), Short Physical Performance Battery (SPPB), Impact of Event Scale-Revised (IES-R).*	**Frequent:** dyspnea 5.5%, ageusia 5%, anosmia 4.6%, arthralgia 5.9%, myalgia 5.9%, severe impairment of lung function <60% of expected 15.5%, mobility limitation 22.3%, any degree of functional impairment 53.8%, Psychological symptoms: mild 25.6%, moderate 11.3%, severe 5.9%.
A8[27]	Quantitative, observational, descriptive documentary study.	Describe the sociodemographic and clinical characteristics of elderly people with COVID-19 sequelae.	Medical records analysis.	The elderly people most affected by post-COVID-19 syndrome were women (58.3%), aged between 60 and 69 years (66.7%), married (49%), with children (64.2%), retired (44.6%) and with an income between two and four minimum wages (33.8%).

A9[28]	Prospective cohort.	Characterize the risk of persistent and new clinical sequelae in adults aged 65 years or older after the acute phase of SARS-CoV-2 infection.	Health plan service records.	**Frequent:** 32% of people had sequelae related to COVID-19. Those who require hospitalization had a markedly increased risk for most clinical sequelae, with the most frequent being: respiratory failure, 26.01%, hypertension, 22.89%, fatigue, 20.36%, kidney problems, 13.08%, and memory problems, 10.99%.
A10[29]	Prospective cohort.	Evaluate the association between SARS-CoV-2 infection and the decrease in Handgrip Strength (HGS).	Evaluation of Hand Grip Strength (HGS) using a digital hand dynamometer.	The level of PMF was not associated with a higher risk of Sars-CoV-2 infection. However, infected individuals showed a decrease of 1.72 kg in the FPM measure, which is 2.27 times more likely when compared to seronegative individuals.
A11[30]	Prospective cohort.	Describe the acute and long-term symptoms of COVID-19 among the elderly and the predictive factors.	Mixed questionnaire with questions related to general and oral health perception, and questions about COVID-19, including vaccination status, time of disease contraction, general and oral symptoms in the acute and persistent phases.	**Frequent:** in women: fatigue 20%, runny nose 13.3%, myalgia and arthralgia 11.7% decreased sensitivity in hands and feet 11.7%. In men: fatigue 15.3%, decreased muscle strength 18.1%, myalgia and arthralgia 13.9%, memory problems 12.5%.

Source: Authors (2024).

Of the research conducted on COVID-19, three were carried out in Italy[22-23,26] and one in each of the countries: France[21], United Kingdom[20], China[24], Egypt[25], Brazil[27], United States[28], Ecuador[29] and Sweden[30]. The largest number of studies originating from the European continent may be related to the higher incidence of COVID-19 cases, as evidenced by updated data available on the WHO dashboard[1]. By the first week of July 2023, the record exceeded 275 million cases.

Regarding the number of deaths, the Americas had already accounted for almost three million in the same period, standing out as leaders in overall mortality from the disease[1]. However, through the search mechanisms used, only three published studies[27-29] were found in American countries for the age group analyzed.

Regarding the typology of the studied population, although the studies focused on the elderly population, there were variations in age limits and proportions between men and women. It also highlights the use of different instruments for data collection, analysis, and clinical history. The studies covered both outpatients with COVID-19 and those who faced more severe cases requiring hospitalization.

DISCUSSION

This integrative literature review on PACS in elderly people highlighted a complex scenario that underscores the unique vulnerability of this population in the pandemic context. The susceptibility of elderly people to COVID-19 and its long-term complications is multifactorial, encompassing biological, social, and environmental aspects, intrinsically linked to the aging process.

The aging process is characterized by a gradual decrease in physiological reserve and an increase in vulnerability to stressors, called immunosenescence[31]. This decline in immune function, associated with a higher prevalence of comorbidities, exposes this population stratum to an elevated risk, not only for severe SARS-CoV-2 infection but also for the development of long-term complications[32-33]. The analyzed studies corroborate this vulnerability, consistently demonstrating that advanced age constitutes a significant risk factor for PACS[29].

Frailty, characterized by increased vulnerability to stressors, can be exacerbated by long COVID[34]. Persistent symptoms of the infection, such as chronic fatigue and muscle weakness, can precipitate the progression from a pre-frail to a frail state[35].

In a state of frailty, affected individuals may experience a slower and incomplete recovery from COVID-19, perpetuating a cycle of functional decline. Chronic inflammation associated with long COVID can potentiate the inflammatory state already present in frailty, worsening negative outcomes[36-37].

The methodological heterogeneity of the studies, although it represents a challenge for the synthesis of evidence, reflects the complex and multisystemic nature of PACS. The geographical diversity of studies - covering various countries is a global phenomenon, raising questions about how different health systems and sociodemographic contexts influence its manifestation and management.

Some studies were conducted with patients hospitalized in intensive care,[20-21,23,26] or who required ventilatory support, while others followed the participants on an outpatient basis[22,24-25].

Significant associations were observed related to the female sex and a higher incidence of PACS[21], greater persistence of symptoms[22], sequelae[27], and a more pronounced worsening in the quality of life score[27], corroborating a study conducted in a population over 18 years old, which showed a higher frequency of fatigue, cough, and dyspnea in women[31].

This consistency across different age groups suggests that biological factors related to sex, such as hormonal and immunological differences, may play a significant role in the response to SARS-CoV-2 and the development of PACS[38]. Additionally, sociocultural factors, such as differences in healthcare-seeking patterns between men and women, have been cited as possible contributors to these observed disparities[39].

Some previous studies have suggested that PACS may potentially accelerate the progression from mild cognitive impairment to dementia in some patients, possibly through mechanisms such as persistent neuroinflammation, cerebral microvascular damage, or exacerbation of underlying neurodegenerative processes[40-42].

The persistent neurological symptoms of COVID-19, such as memory deficits, can mask or overlap with the symptoms of cognitive impairment[40]. In this context,

severe cases of the disease were related to lower cognitive performance compared to non-severe patients and control groups[43-44].

The identified risk factors, such as advanced age, low educational level, presence of comorbidities, severity of COVID-19, ICU admission, and occurrence of *delirium*[24], highlighted the complex interaction between pre-existing vulnerabilities and the impact of acute infection[44-46].

The greater severity and need for hospitalization were more prevalent in the presence of comorbidities and were more associated with increased risks for most post-COVID-19 clinical complications[27-28].

The relevance of social determinants in susceptibility to COVID-19 and the development of PACS in elderly people[30], adds another important layer to the discussion. Factors such as residing in long-term care institutions for the elderly[47], the frequency of social contacts, marital status[48], and educational level influence not only the risk of infection but potentially the course and severity of PACS[49].

The combination of frailty, sarcopenia, and cognitive decline can become even more complex with the addition of persistent COVID-19 symptoms, resulting in an even more heterogeneous clinical presentation[36].

Sarcopenia, characterized by the progressive loss of muscle mass and function, can be significantly aggravated by PACS. Forced physical inactivity during the acute phase of the disease, combined with persistent fatigue and possible malnutrition, can accelerate muscle loss, and become evident from the decline in handgrip strength in post-COVID-19 elderly[29].

The limitations of this review, including the heterogeneity of the studies and the possible selection and language biases, pointed to the need for methodological standardization in future research on PACS in the elderly. The absence of consistent definitions and standardized assessment tools makes it difficult to compare studies and generalize results, a challenge that must be addressed to advance the understanding and management of PACS in this vulnerable population.

CONCLUSION

The results of this review highlight the identification of widely prevalent and common symptoms in elderly people, manifesting in various clinical progressions of COVID-19, which presents a significant potential impact on quality of life. The most common symptoms include dyspnea, fatigue, changes in sleep patterns, and cognitive deficit.

Furthermore, the urgency of conducting new robust clinical studies related to this new health condition is emphasized. These studies aim to establish the most precise definitions of diagnostic criteria, providing a better characterization of symptoms and a more accurate risk stratification. This approach will contribute to more effective guidance in clinical conduct.

Contributions to practice include the development of specific care protocols for elderly people with post-COVID-19 syndrome, ensuring more targeted and effective care. The need to develop personalized intervention strategies is evident, with the aim of improving quality of life and reducing persistent symptoms. Personalized interventions may include physical rehabilitation programs, psychological support, and management of cognitive symptoms. Furthermore, the results can inform public health policies aimed at the prevention and management of post-COVID-19 syndrome in elderly people, promoting the allocation of resources and the development of specialized services.

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Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - **Rodrigues IFA, Silva KHCV e, Stephanus AD, Carvalho LSF de.** Drafting the work or revising it critically for important intellectual content - **Rodrigues IFA, Silva KHCV e, Stephanus AD, Carvalho LSF de.** Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - **Rodrigues IFA, Silva KHCV e, Stephanus AD, Carvalho LSF de.** Definition of theme and methodology - **Rodrigues IFA.** All authors approved the final version of the text.

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