v. 3, n. 17, 2023

International Journal of Health Science

HEART COMPLICATIONS OF COVID-19 IN THE ELDERLY: A LITERATURE REVIEW

Karina Mourão Costa
Social Security Number: 10812036689
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/0998630039800720

Kívia da Silva Joia
Social Security Number: 11647526779
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/4525354798430504

Raphaella Bogado de Bem
Social Security Number: 116.969.466-70
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/1743098152042691

Victoria Domingos Alves Rocha
Social Security Number: 11268051730
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/7308026132498735

Thainá Scramim de Almeida
Social Security Number: 418.226.358-88
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/4707637868574820

Ana Clara Luz Prates Paes Leme
Social Security Number: 059.176.615-96
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/0468467606771114

Andreas Müller Neto
Social Security Number: 170.941.587.85
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/0089236920337187

Alexandra da Silva Barros
Social Security Number: 15492577735
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/6325086343333300

Thaynara Alves de Souza Maciel
09256853647
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/0298990404230123

Patrick de Abreu Cunha Lopes
Student of the Medicine course at the Universidade de Vassouras (UV) and PIBIC scholarship holder for Scientific Initiation at FAPERJ (" Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro")
Vassouras, Rio de Janeiro, Brazil
http://lattes.cnpq.br/9719714143799267

Andressa Atem de Lima Pinheiro
Social Security Number: 672,498,683-49
Resident Doctor in Internal Medicine at the institution: Hospital Escola de Valença (HELGJ)
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/9482108205308655

Ricardo José de Farias Neto
Social Security Number: 008.248.742-18
Doctor specialist in Internal Medicine Ophir Loyola
Valença, Rio de Janeiro, Brazil
http://lattes.cnpq.br/1273592286788242

Abstract: SARS-CoV-2 infection begins in the respiratory system, but the development of systemic diseases accompanied by severe clinical manifestations have also been reported, with dysfunctions of the cardiovascular and immune systems being the main ones. Additionally, the presence of comorbidities and aging represent important risk factors for the severity and poor prognosis of the disease. Since the decline associated with aging has been largely related to the immune system and cardiovascular changes, we sought to investigate the consequences and underlying mechanism of these pathologies to understand the severity of the disease in this population. Understanding-managing the effects of COVID-19 on both systems must translate into medical care for elderly patients with COVID-19, preventing cardiovascular disease and immune changes in this population. Approved therapies that contribute to symptom improvement and mortality reduction, as well as new therapies under development, constitute an approach to manage these disorders. Among them, we describe antivirals, cytokine antagonists, cytokine signalers, nasal pathway inhibitors and vaccines.
Keywords: Coronavirus, COVID-19, mortality, elderly, SARS-CoV-2.

INTRODUCTION

A series of pneumonia cases that occurred in the city of Wuhan in December 2019 led to the eventual identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). 1, 2 Through an epidemiological investigation, the Chinese government narrowed the origin of the virus to the Huanan seafood market in Wuhan. The viral sequence had 96% similarity to a bat coronavirus, and with no evidence of bat-to-human transmission, it was hypothesized that the virus spread to humans via an intermediate host. 1, 3 Genomic sequence studies from Malaysia later suggested that the intermediate hosts were pangolins that were smuggled from Malaysia to China and sold at the Huanan seafood market. 4The subsequent human-to-human spread triggered what later turned into a pandemic.

The World Health Organization (WHO) declared SARS-CoV-2 a pandemic on March 11, 2020. As of March 23, 2020, at 1:25 PM EST, there were 362,019 confirmed cases of SARS-CoV-2 reported in 168 different countries, with 15,488 deaths and a projected total fatality rate (CFR) of 4.3%. 5 The Centers for Disease Control and Prevention (CDC) reported that while individuals over age 65 make up 17% of the total population in the United States, they account for 31% of COVID-19 infections, 45% of hospitalizations, 53 % of admissions to intensive care units and 80% of deaths caused by this infection. 6 This suggests that older individuals are more likely to contract COVID-19 and have worse outcomes compared to the general population.

MATERIAL AND METHODS

A review of the current literature was carried out. The following databases were consulted: MEDLINE (PubMed); Base; Web of Science, Google Scholar. Conference abstracts/papers have been deleted from Embase. No other limits were applied. All retrieved records were organized using Endnote citation management software version 20. To remove duplicates, literature review citation screening and review software was used.

The search strategy was designed to capture the theme in current reviews on elderly and cardiac complications of COVID-19. Searches were complemented by hand searching and retrieving any additional articles that met the eligibility criteria that were cited in our reference lists.

DEVELOPMENT

PATHOPHYSIOLOGY

SARS-CoV-2 spreads by direct transmission, by contact and by aerosol from respiratory droplets and has an average incubation period of 5.1 days. A recent study found that SARS-CoV-2 lasts up to 3 hours in aerosols and remains detectable for up to 72 hours on plastic and stainless-steel surfaces, 24 hours on cardboard and 4 hours on copper. Another possible mode of transmission of SARS-CoV-2 could be through fecal-oral transmission. In a study conducted in 10 pediatric patients with SARS-CoV-2 infections, they continually tested positive for the virus in rectal swabs despite testing negative in nasopharyngeal swabs. Given these findings, patients who test negative on a nasopharyngeal swab may still have an active infection.

The current proposed mechanism for cellular entry is through the angiotensin converting enzyme 2 (ACE-2) receptor found in the lungs, endothelium, heart, kidneys and gastrointestinal system. Spike proteins on the exterior of SARS-CoV-2 anchor the virus to ACE-2 receptors on cells in the lower respiratory tract. This specific mechanism of action may pose a higher risk of infection for older adults. According to the CDC, 63.1% of adults over age 60 have hypertension, 38% of people over age 65 have chronic kidney disease (CKD), and 26.8% of adults over age 65 have diabetes. Many of these patients use ACE inhibitors and angiotensin receptor blockers (ARBs) that upregulate the ACE-2 receptor. Thus, it is hypothesized that older individuals with such comorbidities may be at increased risk and have a more severe course of SARS-CoV-2 infection.

CLINICAL PRESENTATION

The most common presenting symptoms in the general population are fever (98%), cough (76%), dyspnoea (55%), and myalgias or fatigue (up to 44%). These symptoms are also common in older adults; a study of 21 critically ill patients with SARS-CoV-2 infection, mean age 70 years, found that the most common symptoms were shortness of breath (76%), fever (52%) and cough (48%). Up to 86% of the elderly had comorbidities, the most significant being CKD (48%), congestive heart failure (43%), chronic obstructive pulmonary disease (COPD) (33%) and diabetes (33%).

Most older adults have some type of organ damage due to SARS-CoV-2, including acute respiratory illness syndrome (71%), acute kidney injury (20%), heart injury (33%) and liver dysfunction (15%) and 67% required vasopressor support for treatment. In all age groups, chest CT scans of patients with SARS-CoV-2 revealed ground-glass opacities (GGOs) (87%), mixed GBOs and consolidation (65%), vascular dilation (72%), and bronchiectasis of traction (53%). Among these, the lesions presented peripheral distribution (87.1%), bilateral pulmonary involvement (82.2%), inferior pulmonary predominance (54.5%) and multifocality (54.5%). Comparatively, chest X-ray findings in older adults showed bilateral reticular-nodular opacities (58%), OGGs (48%), pleural effusions (about 33%), peribronchial thickening (about 25%), and focal consolidations (about 25%). 20%).

MORTALITY IN THE ELDERLY

Mortality from the SARS-CoV-2 pandemic in older adults was staggering. According to the WHO-China joint fact-finding mission, the overall CFR from 17.3% in January decreased to 0.7% in February, while the CFR in adults aged 80+ increased to 21.9%. Another analysis of 72,314 cases indicated an overall CFR of 2.3%, but a CFR of 8% in patients aged 70 to 79 years and 14.5% in patients older than 80 years. A report on 355 patients with SARS-CoV-2 found that patients who died

had a mean age of 79.5 years. Another report of 4226 cases in the United States indicated a CFR of less than 1% in patients younger than 54 years, but a CFR of 3% to 11% in patients aged 65 to 84 years and 10% to 27% in patients older than 54 years. aged 85. More than 80% of deaths among adult patients occurred in people over 65 years of age. Most fatal cases to date have involved the elderly and patients with comorbidities.

Many older adults in the United States have cardiovascular disease (17%), diabetes (26.8%), hypertension (63.1%), COPD (23.7%) and CKD (38%). An analysis by the WHO-China joint fact-finding mission found that patients over the age of 60 and those with comorbidities were at the highest risk of serious illness and death. The CFR in patients without comorbidities was 1.4%, while the CFR was 13.2% for patients with cardiovascular disease, 9.2% for patients with diabetes, 8.4% for patients with hypertension, 8% for patients with chronic respiratory disease and 7.6% for patients with cancer. 19 A study of 46 fatal cases of SARS-CoV-2, in which 84% of patients were over 60 years old, found that diabetes is likely to be associated with increased mortality. Another study of critically ill elderly patients with SARS-CoV-2 found that 86% of patients had comorbid conditions such as CKD, congestive heart failure, COPD, and diabetes. This likelihood of having multiple comorbidities puts older adults at an even greater risk of increased mortality from SARS-CoV-2.

SARS-COV-2 AND CARDIOVASCULAR CHANGES

Patients suffering from COVID-19 often experience respiratory distress accompanied by, among other signs and symptoms, an excessive inflammatory response and vascular complications that lead to damage to multiple organs, which constitutes a major threat. Interestingly, cardiovascular changes without signs of respiratory disorders have been reported. In addition, respiratory symptoms are worse in patients with COVID-19 in the setting of chronic cardiac disorders. Consequently, SARS-CoV-2 has been found to interact with and affect the cardiovascular and ocular system by attaching itself to host cells via the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed not only in the lungs but also in other tissues, including the heart and endothelium. This interaction leads to microvascular dysfunction8, among other alterations. Likewise, TMPRSS2, cathepsin L and furin, proteins involved in the priming process that viral S protein undergoes to facilitate SARS- CoV-2 binding to its cognate ACE2 receptor, is also expressed in the decoronary endothelium as well as in cardiomyocytes. Among the cardiovascular alterations, patients with COVID-19 commonly present disc injury, with or without clinical manifestations. Although hypoxia, left ventricular weakening (Takotsubo syndrome), endothelial damage and vascular dysfunction, myocarditis, and a systemic inflammatory response known as a cytokine storm underlie the disparate effects of SARS-CoV-2 infection in patients with and without cardiovascular comorbidities, its mechanisms and contributions remain incompletely understood. A large body of evidence suggests that patients with severe symptoms often have complications that lead to cardiomyocyte death, thus involving myocardial damage. A comprehensive meta-analysis revealed that the incidence of myocardial damage increased to 30% in patients older than 60 years, twice as much as in younger patients. Injury repair is performed primarily by determining levels of the circuit biomarker troponin and, more precisely, the high-sensitivity cardiac troponin I (hs-cTnI) isoform. Between 10 and 30% of patients requiring treatment in health

facilities have heart problems and increased troponin levels. It is widely accepted that the higher the troponin level, the worse the prognosis. Thus, elevated troponin levels are highly associated with increased mortality, even though patients do not have suggestive acute coronary syndrome. Similarly, elevation of N-terminal B-type natriuretic peptide (NT-pro) BNP, creatine phosphate, markers of cardiac injury phokinase (CK)-MB, and myoglobin (MYO) above established thresholds off, a measure of cardiomyocyte death, was associated with an increased risk of death. However, these markers are not capable of distinguishing between different causes responsible for myocardial damage, which includes, among others, myocarditis, cardiomyopathy and myocardial infarction. Since the identification of the first small (17-25 nucleotides) non-coding RNAs in 1993, microRNAs (miRNAs) have become a valuable tool in the field of research, being involved in several cardiovascular changes, including cardiac hypertrophy, heart disease and heart failure., among others. Furthermore, since their identification in the circulatory system, miRNAs have been considered not only a potential biomarker, but also a plausible therapy against hepatitis C virus (Miravirsen) infection. Importantly, a recent review that focused on the role of miRNAs in complications associated with COVID-19 sheds light on their potential as valuable markers and predictors of cardiac and vascular damage in SARS-CoV-2 infection. Furthermore, the authors discuss their usefulness as potential therapeutic targets for patients with COVID-19.

MYOCARDITIS AND INFLAMMATORY CARDIOMYOPATHY

Since the first report detecting the SARS-CoV-2 genome in cardiac biopsies from patients diagnosed with myocarditis or explained heart failure, many case studies have identified this alteration in patients with COVID-19. However, reports rarely demonstrate this clinical condition regardless of its origin. All analyzed tissues exhibiting high copy numbers demonstrated increased levels of pro-inflammatory cytokines (TNF-α; IFN-γ; CCL5; and IL-6, -8, and -18) versus non-patients with cardiac infection. Myocarditis was observed mainly, but not exclusively, in the group of young male adults (18 to ≤64 years old), whose symptoms resolved in the short term without sequelae. This unexpected pattern of adverse events necessitates a larger randomized trial, particularly in the long term, to assess safety in this more vulnerable elderly population.

CARDIAC INSUFFICIENCY

According to the results observed in two independent retrospective studies performed on patients with COVID-19 in China, heart failure was the most common complication not involving the respiratory system. It is important to emphasize that this manifestation was associated with higher mortality during hospitalization when compared to survivors. Recently, a follow-up study covering a large cohort of COVID-19 patients in the US sheds light on long-term cardiovascular outcomes. The authors estimated cardiovascular risks beyond the first month after infection and demonstrated an increased risk of several cardiovascular changes, regardless of whether patients were hospitalized or not. The increased risk was most pronounced for heart failure, followed by atrial fibrillation, regardless of the presence of other cardiovascular risk factors. Although the authors suggest that SARS-CoV-2 infection can also lead to the appearance of a new cardiovascular disease, whether the heart failure arises due to an aggravation of pre-existing pathology or due

to a new cardiac dysfunction, as shown above, remains uncertain, necessitating further efforts to address health strategies that will be needed to treat those affected.

CARDIOGENIC SHOCK

This represents a common cause of mortality caused by severely compromised myocardial outcomes, leading to hypoxia, hypoperfusion, and decreased cardiac output. Hypoxia, excessive inflammatory response, vasodilation, and shock as the SARS-CoV-2 infection progresses may underlie this fatal condition. They are aggravated by pre-existing cardiovascular dysfunction. A case study demonstrated that elevated levels of SARS-CoV-2 antibodies may play a pathogenic role in the hyperinflammatory response. This virus-host interaction appears to facilitate viral entry mediated by an antibody-dependent enhancement mechanism, as we will explain later. Signs and symptoms resolved quickly after treatment with a moderate dose of steroids in this population. More importantly, elderly patients with cardiogenic shock have a shorter survival, along with a higher risk of death.

CARDIAC ARRHYTHMIAS

A multicenter study conducted in hospitalized patients with COVID-19 observed a variety of arrhythmic manifestations, ranging from benign to potentially life-threatening, with sinus tachycardia (rate > 100 beats per minute) being the most common. Heart rhythm changes were mostly reported in patients with COVID-19 who were transferred to the intensive care unit, with 44.4% versus 16.7% of patients not requiring intensive care. More recently, a meta-analysis involving the small number of studies on bradycardia and mortality in patients with COVID-19 showed that bradycardia was not statistically associated with mortality in patients with COVID-19. In the context of a viral infection, different factors have been associated with this outcome. Upregulation of the cognate viral receptor ACE2 in cardiac tissue may facilitate entry into the conduction system, leading to arrhythmia. Medications that prolong the QT segment, hypoxia and electrolyte disturbances, a pro-inflammatory state, metabolism and cardiovascular comorbidities or complications in the context of an oral infection can also trigger cardiac dysrhythmia more easily.

ACUTE MYOCARDIAL INFARCTION

Fortunately, most COVID-19 patients have mild symptoms or are asymptomatic. However, more severe clinical manifestations, including pneumonia and acute respiratory distress, are aggravated in elderly patients, diagnosed or not, with cardiac and/or cardiovascular impairment. Elevated troponin levels are common in COVID-19 patients hospitalized due to stress cardiomyopathy, ischemia, or systemic release of inflammatory cytokines. A minority of them have symptoms and signs suggestive of acute coronary syndrome. In addition, cardiovascular diseases, obesity and diabetes increase the risk of poor prognosis, with patients with myocardial injury having the worst prognosis. According to a comprehensive review, the frequency of myocardial injury varies widely, ranging from 7 to 28%, and there is a strong correlation between myocardial injury and disease severity. Signs and symptoms were more pronounced in patients suffering from previous cardiovascular disease and in the elderly.

STRESS CARDIOMYOPATHY

This condition, also known as Takotsubo syndrome, develops after intense emotional or physical stress, leading to acute but reversible left ventricular failure. Affected people

have similar symptoms (altered echo and electrocardiogram). Profiles to those seen in myocardial infarction but without obstructive coronary artery disease. The first systematic review in patients with COVID-19 (mean age 70.8 years) concluded that inflammation (cytokine storm and cardiovascular comorbidities) and physical (intubation) and/or emotional stress (social isolation and associated anxiety) underlie the syndrome, which was predominant in older women. The absence of major coronary lesions almost ruled out the role of acute coronary syndrome as the primary cause of Takotsubo syndrome. This study covered a small number of patients, and some of them were recommended to be excluded from the systematic review. More studies are needed to shed light on this topic.

COAGULATION ABNORMALITIES

Patients infected with SARS-CoV-2 demonstrate a wide range of coagulation abnormalities accompanied by increased levels of thrombotic factors such as factor VIII, fibrinogen and prothrombotic microparticles. Likewise, elevated neutrophil counts and levels of D-dimer, a breakdown product of cross-linked fibrin indicative of increased thrombin generation and fibrin dissolution, have been reported. Together, coagulation abnormalities can lead to thrombosis and embolic events, a common complication in critically ill patients with COVID-19, whether in veins or arteries. The ability of the virus to directly infect endothelial cells is the basis of cell damage and therefore may explain the large number of effects reported in patients with COVID-19, such as vascular micro-inflammation, endothelial exocytosis and endothelitis.

COVID-19 AND THE IMMUNE SYSTEM IN THE ELDERLY

Various risk factors such as age, male gender, obesity, smoking, hypertension, diabetes mellitus have been reported to influence the development of severe cases of COVID-19. Age is considered the most relevant, as we have already noted, not only for the development of COVID-19, but also for its adverse health outcomes. Therefore, the dysregulation of the immune system that occurs during the aging process may contribute to the opathogenesis of the disease. In 2020, at the beginning of the pandemic, SARS-CoV-2 was a new pathogen, and the entire population was unprotected because there was no herd immunity.

INNATE RESPONSE AND INFLAMMATION IN COVID-19 IN OLDER ADULTS

The severity of the disease is marked not only by the virus itself, but also by an aberration in the intense immune response. Three different phases have been clinically described. First, an immune response against the virus, triggering an inflammatory response. Symptoms include fever, dry cough, diarrhea and headache, which may be complicated in a second phase by dyspnea and hypoxia. In the worst cases, the third stage, acute respiratory illness (ARDS), develops, requiring intubation and ventilatory support and occasionally causing multiorgan failure and death.

FINAL CONSIDERATIONS

Older adults (60 years and older) commonly have cardiovascular complications and associated comorbidities. In myocardial injury, the most common complication, can be explained or be associated with myocarditis, stress and myocardial cardiomyopathy. Specifically, more research is needed to clearly establish the relationship between myocardial injury and viral infection. Furthermore, its contribution to the inflammatory state compared to those caused by other respiratory viruses will help to understand the

differential symptoms and observed severity. Furthermore, deficiencies in the activation of the innate/adaptive immune response due to age and/or virus-related factors have been described. The pairing that occurs physiologically in older adults leaves them in a state with an induced immune response against pathogens and, in particular, SARS-CoV-2 infection. Studies exploring why there is bias towards a humoral response, therefore, the effective elimination of the virus by the cytotoxic response, must be studied further, as well as the role that macrophages play in the inflammatory response, the cytokine storm and tissue damage. As more and more evidence of the long-term effects of COVID-19 is emerging, it is essential to know whether vaccines will help prevent the aforementioned cardiac complications (heart failure, arrhythmias) as well as the impact they will have on orchestrating an effective immune response macrophages, T and B lymphocytes and other immune cells, towards an effective and lasting response over time. Ongoing clinical trials will assess the safety and efficacy of new therapeutic strategies capable of preventing and reducing the high mortality rate.

REFERENCES

PIVA, Tommaso et al. Exercise program for the management of anxiety and depression in adults and elderly subjects: Is it applicable to patients with post-covid-19 condition? A systematic review and meta-analysis. **Journal of Affective Disorders,** 2023.

GHASEMI, Hoomaan et al. Takotsubo syndrome and COVID - 19: A systematic review. **Health science reports,** v. 6, no. 1, p. e972, 2023.

KAPUSTA, Joanna et al. Do selected lifestyle parameters affect the severity and symptoms of COVID-19 among elderly patients? The retrospective evaluation of individuals from the STOP-COVID registry of the PoLoCOV study. **Journal of Infection and Public Health,** v. 16, no. 1, p. 143-153, 2023.

WATANABE, Atsuyuki et al. Assessment of Efficacy and Safety of mRNA COVID-19 Vaccines in Children Aged 5 to 11 Years: A Systematic Review and Meta-analysis. **JAMA pediatrics,** 2023.

INZITARI, Marco et al. Comprehensive Geriatric Hospital At Home: adaptation to referral and case-mix changes during the COVID-19 pandemic. **Journal of the American Medical Directors Association,** v. 24, no. 1, p. 3-9. e1, 2023.

OKOYE, Chukwuma et al. Determinants of 1-Year Adverse Event Requiring Re-Hospitalization in COVID-19 Oldest Old Survivors. **Geriatrics,** v. 8, no. 1, p. 10, 2023.

VAN DER SLUIJS, Koen M. et al. Long-term cardiovascular health status and physical functioning of nonhospitalized patients with COVID-19 compared with non-COVID-19 controls. **American Journal of Physiology-Heart and Circulatory Physiology,** v. 324, no. 1, p. H47-H56, 2023.

YUSHARYAHYA, Shannaz Nadia et al. Cutaneous manifestations in elderly patients with confirmed coronavirus disease 2019 and the disease outcomes: A systematic review. **The Journal of Dermatology.**

PAPAZACHARIOU, Andria et al. The impact of seasonal influenza vaccination uptake on COVID-19 vaccination attitudes in a rural area in Greece. **Vaccine,** v. 41, no. 3, p. 821-825, 2023.

REVU, J. et al. non-communicable disease management: Access to healthcare during COVID-19 pandemic in rural Kerala, India. **Clinical Epidemiology and Global Health,** v. 20, p. 101231, 2023.

RIVERA-TORRES, José; GIRON, Natalia; SAN JOSÉ, Esther. COVID-19: A Comprehensive Review on Cardiovascular Alterations, Immunity, and Therapeutics in Older Adults. **Journal of Clinical Medicine,** vol. 12, no. 2, p. 488, 2023.

MERTEN, Natascha et al. Psychological Distress and Well-Being Among Sensory Impaired Individuals During COVID-19 Lockdown Measures. **Annals of Epidemiology,** 2023.

GRUISKENS, Jeroen RJH et al. The psychosocial impact of the COVID-19 pandemic on chronic care patients. **Journal of the American Medical Directors Association,** 2023.

ZUIN, Marco et al. Risk of venous thromboembolic events after COVID-19 infection: a systematic review and meta-analysis. **Journal of Thrombosis and Thrombolysis,** p. 1-9, 2023.

AMRAM, Daniel L. et al. COVID-19: tobacco smoking and other risk factors in the elderly. **JOURNAL OF GERONTOLOGY AND GERIATRICS,** p. 1-7, 2023.

MASSARI, Maria Chiara et al. Nutritional and physical activity issues in frailty syndrome during the COVID-19 pandemic. **Therapeutic Advances in Musculoskeletal Disease,** v. 15, p. 1759720X231152648, 2023.

MENDITTO, Alessio et al. Admission high-sensitivity cardiac troponin levels as a prognostic indicator for in-hospital mortality rates in the elderly and very elderly COVID-19 patients. **Archives of gerontology and geriatrics,** v. 104, p. 104822, 2023.

FERICEAN, Roxana Manuela et al. Outcomes of Elderly Patients Hospitalized with the SARS-CoV-2 Omicron B. 1.1. 529 Variant: A Systematic Review. **International Journal of Environmental Research and Public Health,** v. 20, no. 3, p. 2150, 2023.

SZYCHOWSKA, Agnieszka et al. Physical Activity versus Selected Health Behaviors, Subjective Physical and Psychological Health and Multimorbidity in a Large Cohort of Polish Seniors during the COVID-19 Pandemic (Results of the National Polish Health Test). **International Journal of Environmental Research and Public Health,** v. 20, no. 1, p. 556, 2023.

DADRAS, Omid et al. COVID - 19 mortality and its predictors in the elderly: A systematic review. **Health science reports,** v. 5, no. 3, p. e657, 2022.

PÉTERFI, Anna et al. Comorbidities and increased mortality of COVID-19 among the elderly: a systematic review. **Physiology international,** 2022.

PEPERA, Garyfallia et al. Epidemiology, risk factors and prognosis of cardiovascular disease in the Coronavirus Disease 2019 (COVID-19) pandemic era: A systematic review. **Reviews in Cardiovascular Medicine,** v. 23, no. 1, p. 28, 2022.

SENIA, Paola et al. Survey on COVID 19related mortality associated with occupational infection during the first phase of the pandemic: A systematic review. **Experimental and Therapeutic Medicine,** v. 23, no. 1, p. 1-16, 2022.

LAZZARI, Carlo; RABOTTINI, Marco. COVID-19, loneliness, social isolation and risk of dementia in older people: a systematic review and meta-analysis of the relevant literature. **International Journal of Psychiatry in Clinical Practice,** v. 26, no. 2, p. 196-207, 2022.

JOLI, Jian et al. post-COVID-19 fatigue: A systematic review. **Frontiers in Psychiatry,** v. 13, 2022.