Main complications of covid-19 and future implications: integrative review

Principais complicações da covid-19 e implicações futuras: revisão integrativa

Principales complicaciones del covid-19 y futuras implicaciones: revisión integrativa

ABSTRACT
Objective: to synthesize the scientific evidence regarding the main complications of COVID-19, during the period of convalescence, in adult and elderly patients. Method: integrative review carried out between March and May 2021 in the sources: US National Library of Medicine National Institutes Database Search of Health, Latin American and Caribbean Literature in Health Sciences, Scopus, Cumulative Index to Nursing and Allied Health Literature, Web of Science, Excerpta Medical Database. The Rayyan software was used for selection and analysis of content. Results: 833 articles were identified and nine of them comprised the sample. Complications were of neurological, respiratory, psychiatric, cardiovascular, nutritional and muscular nature. Conclusion: the most important complications of COVID-19 were respiratory and neurological disorders, which imply an increase in decompensated patients in health services seeking elective procedures, increased public spending, and incidence of out-of-hospital cardiac arrest.
Descriptors: Follow-Up Studies; Coronavirus Infections; Nursing; Adult; Elderly.

RESUMO
Descritores: Seguimentos; Infeções por Coronavírus; Enfermagem; Adulto; Idoso.

RESUMEN
Descripciones: Estudios de Seguimiento; Infecciones por Coronavirus; Enfermería; Adulto; Anciano.

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1University of Uberaba, Uberaba – MG, Brazil
2Federal University of Minas Gerais, Belo Horizonte – MG, Brazil

Corresponding author:
Fabiana Cristina Pires Bernardinelli
E-mail: enfermagem.pires@gmail.com
INTRODUCTION

Since the beginning of time, humanity has been plagued by a variety of contagious diseases that weaken the health of the population, cause high levels of morbidity and mortality, socioeconomic disruptions, suffering, but also advances in science\(^{(1)}\). This context is reinforced by an emerging disease caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus, known worldwide as COVID-19\(^{(2)}\).

First identified in the Chinese province of Wuhan, specifically in a wild animal sales market in December 2019, COVID-19 spread rapidly around the world in the year 2020 and became a pandemic in little more than two months\(^{(3)}\).

Transmitted through the air or by contact with contaminated secretions, such as droplets of saliva, sneezing, coughing, lung secretions, close personal contact, with contaminated objects or surfaces, followed by contact with the mouth, nose or eyes, the COVID-19 virus, considered highly pathogenic, invades the human organism and remains incubated for an average of five days, when the first symptoms of acute respiratory syndrome appear\(^{(2)}\).

The initial symptomatology varies from individual to individual, manifested in a milder form, such as a cold associated with malaise, hyperthermia, fatigue, cough, dyspnea, anorexia, sore throat, headache, diarrhea, nausea and vomiting, or in more striking forms, such as pneumonia, severe pneumonia and Severe Acute Respiratory Syndrome (SARS), capable of causing a variety of complications, addressed by the scientific literature\(^{(2-4)}\).

Despite the unprecedented global effort, in terms of scale and speed, to intensify research and knowledge on COVID-19, the exploration of its complications has been occurring in a fragmented way, that is, the studies produced in this area, address one type of complication at a time, describing it accurately. In this way, it is possible to affirm that there is still no scientific production, which proposed to compile, in a single manuscript, the main complications of COVID-19, analyze them and reflect on their implications for the future to support the clinical practice of health professionals, especially nurses; this fact causes a difficulty in providing safe, correct and quality care based on scientific evidence and protocols in order to ensure effective care\(^{(5)}\).

Obtaining studies that identify and synthesize knowledge about the main complications arising from COVID-19 can encourage and speed up the dissemination of this knowledge, with greater breadth in the analysis of evidence, and support the determination of best care practices for safety of patients affected by COVID-19, specifically with regard to nursing practice; the knowledge produced here can support better clinical decision-making, from the moment it synthesizes the main complications arising from this disease, as well as managerial actions, subsidizing the construction of care protocols and consequent training of the health team, for the correct management of complications\(^{(4-5)}\). In view of the above, the question is: what are the main complications that can manifest in adult and elderly patients infected by COVID-19 during the period of convalescence? This study aimed to synthesize the scientific evidence regarding the main complications of COVID-19 which occurred during the period of convalescence in adult and elderly patients.

METHOD

This is an integrative literature review to establish the synthesis and analysis of the scientific knowledge already produced on the complications of COVID-19, supported by the Statement for Reporting Systematic Reviews and Meta-Analyses of Studies (PRISMA), a reference composed of a 27-item checklist and a four-stages flowchart, capable of conferring quality on review studies\(^{(6)}\).

Six stages were carried out in this review: (1) definition of the research question; (2) establishment of inclusion and exclusion criteria for the literature search; (3) definition of the information extracted from the studies; (4) evaluation of included studies; (5) interpretation of results; and (6) synthesis of data\(^{(7)}\).

In the first stage, after determining the research topic, the Population - Interest Phenomenon - Context (PI(\(\text{Co}\))\(^{(8)}\) strategy was adopted to elaborate the guiding question, configured by the acronym P (Population), represented by adult and elderly patients, acronym I (Intervention), the synthesis of the main complications of COVID-19, and the acronym Co (Context), convalescence, that is, the period of recovery after COVID-19. The following question was posed: what is the scientific evidence present in the literature on the main complications that may emerge during the period of convalescence after COVID-19 in adult and elderly patients?

In the second stage, the inclusion and exclusion criteria were defined for the selection of manuscripts, prioritizing primary studies that
addressed some type of complication caused by COVID-19, in the adult and elderly population, during the period of convalescence, with a time established from December 2019, given the emergence of COVID-19, and without limitation of language. Studies such as literature review, letter to the editor, editorials, theses, dissertations, opinion articles, comments, essays, previous notes, manuals, books and book chapters were excluded.

The following sources of information were used: (1) US National Library of Medicine National Institutes Database Search of Health (Medline/PubMed®); (2) Scopus; (3) Cumulative Index to Nursing and Allied Health Literature (CINAHL); (4) Web of Science; (5) Excerpta Médica Database (Embase) and (6) Latin American and Caribbean Literature on Health Sciences (LILACS).

The search for evidence took place in March 2021, combining the elements of the PICO strategy, Boolean operators and search codes, specific to each source, since each one works in a unique way and responds to different commands, which implies the adaptation of the strategy, as described in box 1, below:

Box 1 – Descriptors, keywords and search strategy used in this integrative review. Uberaba, MG, Brazil, 2021.

<table>
<thead>
<tr>
<th>Source of information</th>
<th>Descriptors, keywords and search strategies</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PubMed®</strong></td>
<td>Controlled descriptors, in English, identified in the Medical Subjects Headings (MeSH) were adopted: Patients; Adult; Aged; COVID-19; “post-acute COVID-19 syndrome”; Convalescence and the keyword: Complication. The following strategy was used: ((Patients OR Patient) OR (Clients OR Client) AND (Adult OR Adults) AND (Aged OR Elderly) AND (Complication OR “post-acute COVID-19 syndrome”) AND (COVID-19) AND (Convalescence OR Convalescences)).</td>
</tr>
<tr>
<td><strong>SCOPUS</strong></td>
<td>Controlled descriptors, in English, identified in the Medical Subjects Headings (MeSH) were used: Patients; Adult; Aged; COVID-19; “post-acute COVID-19 syndrome”; Convalescence and the keyword: Complication. The following strategy was used: TITLE-ABS-KEY((Patients OR Patient) OR (Clients OR Client) AND (Adult OR Adults) AND (Aged OR Elderly) AND (Complication OR “post-acute COVID-19 syndrome”) AND (COVID-19) AND (Convalescence OR Convalescences)).</td>
</tr>
<tr>
<td><strong>CINAHL</strong></td>
<td>Controlled descriptors were identified in Titles/Subjects, in English: Patients; Adult; “Aged, Hospitalized”; COVID-19; “Coronavirus Infections”; Recovery and the keyword: Complication. The strategy was carried out: (Patients AND Adult AND “Aged, Hospitalized” AND “COVID-19” OR “Coronavirus Infections” AND Complication AND Recovery).</td>
</tr>
<tr>
<td><strong>Web of Science</strong></td>
<td>The following descriptors were adopted in English: Patients; Adult; “Aged, Hospitalized”; COVID-19; “Coronavirus Infections”; Recovery and the keyword: Complication. The following strategy was used: TS=(Patients AND Adult AND “Aged, Hospitalized” AND “COVID-19” OR “Coronavirus Infections” AND Complication AND Recovery).</td>
</tr>
<tr>
<td><strong>LILACS</strong></td>
<td>We opted for the controlled descriptors present in the Health Sciences Descriptors (DeCS) in Portuguese, English and Spanish. The English version is shown here: Adult; Aged; COVID-19 and the keyword: Complication. Two strategies in English were used: (Adult) AND (Complication) AND (COVID-19) AND (Aged) AND (Complication) AND (COVID-19), accompanied by their versions in Spanish and Portuguese.</td>
</tr>
<tr>
<td><strong>Embase</strong></td>
<td>Controlled descriptors in English were used: Patients; Adult; “Aged, Hospitalized”; COVID-19; “Coronavirus Infections”; Recovery and the keyword: Complication. The following strategy was used: (Patients AND Adult AND “Aged, Hospitalized” AND “COVID-19” OR “Coronavirus Infections” AND Complication AND Recovery).</td>
</tr>
</tbody>
</table>

Manuscripts identified in the search were exported from the sources of information to a free online single-version review software called the Rayyan Qatar Computing Research Institute (Rayyan QCRI), available at: https://rayyan.qcri.org, capable of excluding duplicate articles, facilitating the initial screening, blinding the auxiliary researcher and incorporating a high level of usability and effectiveness in the study selection process³⁹.

Then, the selection of studies was carried out in Rayyan, a priori, by the reading of titles and abstracts by two independent researchers. There was divergence of selection among the researchers, so 36 articles were sent to a third researcher, responsible for the decision to include them or not in the sample.

Subsequently, the selected articles were read in full and the final sample was defined. It should be noted that a search was carried out in

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In the third stage, information relevant to the research question was extracted from the studies using a validated instrument\(^{(10)}\), considering the following criteria: author, year of publication, country of origin, objective, type of study, results/conclusions, and finally, the level of evidence of the studies was classified\(^{(11)}\). The level of evidence was classified into seven categories, namely: level 1: systematic review or meta-analysis; level 2: randomized controlled clinical trial; level 3: well-designed clinical trials without randomization; level 4: well-designed cohort and case-control studies; level 5: systematic review of descriptive and qualitative studies; level 6: descriptive or qualitative study; level 7: opinion of authorities and/or report of expert committees\(^{(11)}\).

The fourth stage of the research protocol addressed the analysis and categorization of the findings, through Thematic Analysis\(^{(12)}\), carried out in three stages: pre-analysis, consisting of the skimming of the evidence and organization of the convergent information, and the exploration of the material, with grouping of convergences and data treatment, listing the categories. Then, the fifth and sixth stages were carried out, consisting in the interpretation of results and synthesis of knowledge. In accordance with the ethical and legal aspects of Resolution number 466/2012\(^{(13)}\), the research was not submitted to the Research Ethics Committee (REC) as it was a literature review and did not involve human beings.

RESULTS

Initially, 833 studies were identified, and nine composed the final sample of this research. The selection process is shown in Figure 1, below.

The studies were published in 2020, internationally, and characterized, for the most part, by level 6 of evidence. Two categories were developed: (A) Characterization of the complications of COVID-19 in adults and the elderly during the period of convalescence and (B) future implications of the complications of COVID-19 for patients and the health system.

(A) Characterization of the complications of COVID-19 in adults and the elderly during the period of convalescence: six main types of complications were identified: (1) neurological complications - acute encephalopathy, stroke, delirium, headache, anosmia, seizures, meningitis, neuropathy, encephalitis, coma, myelopathy, polyneuropathy, neuropathy, dizziness, impaired consciousness, agitation, confusion\(^{(16-17,20,22)}\) (2) respiratory complications - respiratory failure, acute pulmonary embolism\(^{(14-15,18-19)}\) (3) psychiatric complications - anxiety, insomnia, mood disorders and suicidal ideation\(^{(14,17)}\) (4) cardiovascular complications - heart failure, arterial hypertension\(^{(18)}\) (5) nutritional complications - malnutrition, anorexia\(^{(14,21-22)}\) and (6) muscular complications – myalgia, pain\(^{(17)}\).

Among these, respiratory\(^{(14-15,18-19)}\) and neurological complications stood out, with a predominance of encephalopathy and stroke\(^{(16-17,20,22)}\). The outcome of death was mainly acute pulmonary embolism\(^{(18)}\), delirium\(^{(16)}\) and heart failure\(^{(15)}\).

(B) Future implications of COVID-19 complications for patients and the healthcare system: (1) increased patient demand and healthcare structuring needs; (2) sudden increase in elective procedures after the pandemic, in the number of decompensated patients, secondary to non-adherence to treatments, overload of the health system and increased public spending; (3) increased incidence of out-of-hospital cardiac arrest and death\(^{(14,16)}\).
Figure 1 – Flowchart of identification, selection and inclusion of studies, based on the recommendation of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Uberaba, MG, Brazil, 2021.

Box 2 presents the characterization of the studies included in the sample.

CINAHL: Cumulative Index to Nursing and Allied Health Literature; LILACS: Latin American and Caribbean Literature in Health Sciences.

Source: data from this survey, 2021.
Box 2 – Characterization of the studies that made up the sample of the integrative literature review. Uberaba, MG, Brazil, 2021.

<table>
<thead>
<tr>
<th>Authors/year of publication/ country of origin</th>
<th>Objective and type of study</th>
<th>Results/conclusion and level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lorenzo et al., 2020&lt;sup&gt;14&lt;/sup&gt; Italy</td>
<td>To investigate the residual dysfunctions of COVID-19. Cohort study.</td>
<td>Of the 185 patients included, 31.3% had dyspnea, 22.2% tachypnea, 5.4% malnutrition, 57.3% risk of malnutrition. 21.6% patients had uncontrolled blood pressure and 25.4% recent onset cognitive impairment. Post-traumatic stress disorder was observed in 22.2% patients. It was concluded that COVID-19 may cause physical and psychological impairment, and increased long-term morbidity and mortality. Level of evidence 4.</td>
</tr>
<tr>
<td>Ran et al., 2020&lt;sup&gt;15&lt;/sup&gt; China</td>
<td>To estimate the risks of adverse events in COVID-19 hypertensive patients. Cohort study.</td>
<td>Of the 803 patients, 8.3% were hypertensive, 3.7% had respiratory failure, 3.2% had heart failure, and 4.8% died. 17.6% had poor BP control during hospitalization. It was concluded that poor BP control is directly associated with complications in patients who had COVID-19. Level of evidence 4.</td>
</tr>
<tr>
<td>Ticinesi et al., 2020&lt;sup&gt;16&lt;/sup&gt; Italy</td>
<td>To identify the clinical correlates of COVID-19 and the association with mortality. Descriptive study.</td>
<td>Of the 852 patients, 11% developed delirium during hospital stay. Patients with delirium were older, had cough less frequently, had atypical symptoms such as syncope, postural instability, and chest pain, and presented oxygen saturation values. It was concluded that delirium was associated with higher mortality, and noted as a marker of severe COVID-19. Level of evidence 6.</td>
</tr>
<tr>
<td>Nalleballe et al., 2020&lt;sup&gt;17&lt;/sup&gt; USA</td>
<td>To analyze adult patients with COVID-19 who had neuropsychiatric complications. Descriptive study.</td>
<td>Among the 9,086 patients evaluated, headache, sleep disorders, encephalopathy, stroke, transient ischemic attack, and seizures were detected, as well as anxiety and other related disorders, mood disorders, and suicidal ideation. It was concluded that early recognition and prompt management of neuropsychiatric complications have the potential to decrease morbidity and mortality. Level of Evidence 6</td>
</tr>
<tr>
<td>Chen et al., 2020&lt;sup&gt;18&lt;/sup&gt; China</td>
<td>To describe possible complications in patients with COVID-19 and clinical features of acute pulmonary embolism. Descriptive study.</td>
<td>Twenty-five (25) COVID-19 patients who underwent CT scan were analyzed, most patients had some symptoms related to suspected acute pulmonary embolism (20 with dyspnea, 4 with chest pain, and 4 with hemoptysis). It was concluded that patients who have COVID-19 are at risk of developing acute pulmonary embolism. Level of Evidence 6.</td>
</tr>
<tr>
<td>Mestre-Gómez et al., 2020&lt;sup&gt;19&lt;/sup&gt; Spain</td>
<td>To evaluate the cumulative incidence of pulmonary embolism (PE) in COVID-19 patients. Descriptive study.</td>
<td>A total of 452 electronic medical records were analyzed, 31.9% were diagnosed with acute pulmonary embolism. All were classified as COVID-19 infection. It was concluded that elderly, male, and patients with comorbidities were more likely to develop pulmonary embolism. Level of evidence 6.</td>
</tr>
<tr>
<td>Frontera et al., 2020&lt;sup&gt;20&lt;/sup&gt; USA</td>
<td>To characterize and estimate the prevalence of neurological syndromes in patients with COVID-19. Descriptive study.</td>
<td>It was found that 84% of patients with COVID-19 had neurological symptoms, including encephalopathy, agitation and confusion, and corticospinal tract signs. It was concluded that from a global survey it was possible to identify the prevalence of acute neurological events. Level of Evidence 6.</td>
</tr>
<tr>
<td>Li et al., 2020&lt;sup&gt;21&lt;/sup&gt; China</td>
<td>To evaluate the prevalence of malnutrition and its related factors in elderly patients with COVID-19. Descriptive study.</td>
<td>A total of 182 patients were evaluated, 52.7% were malnourished, and 27.5% were at risk of malnutrition. It was concluded that there was a high prevalence of malnutrition in elderly patients diagnosed with COVID-19, which reinforces the need for nutritional support. Level of Evidence 6.</td>
</tr>
<tr>
<td>Zabihi et al., 2020&lt;sup&gt;22&lt;/sup&gt; Iran</td>
<td>To investigate the neurological manifestations of COVID-19. Descriptive study.</td>
<td>Of the 230 patients evaluated with COVID-19, complications such as headache, dizziness, impaired consciousness, seizure, stroke, taste impairment, smell impairment, fever, cough, and anorexia were detected. In addition, they presented musculoskeletal lesions. It was concluded that neurological manifestations are substantial in patients with COVID-19. Level of Evidence 6.</td>
</tr>
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</table>

Source: data from this survey itself, 2021.
DISCUSSION

The complications caused by COVID-19 are characterized by varied clinical conditions capable of negatively impacting the survival and quality of life of adult and elderly patients affected by this disease\(^{(14)}\).

The selected study sample was mostly supported by manuscripts with evidence level 6, characterized by observational and descriptive studies, which, \textit{a priori}, is recommended given the contemporaneity of the COVID-19 theme, and the consequent need to initially, explore and understand this context, and only then develop other studies that, by appropriating this framework of knowledge, will be able to carry out correlations, associations and comparisons\(^{(11)}\).

This research gives the science of health and nursing an originality, by compiling the knowledge produced on the complications of COVID-19, in a single study, aimed at adult and elderly patients, identifying the complications that overlap in the literature and highlighting the main future implications of this context, for the patient and the health system, subsidizing the reflection and decision-making of health professionals, specifically, nurses, for a more assertive clinical practice, facing the needs of this population, and the conditions that may emerge from this scenery. In addition, such results provided support to these professionals to develop protocols, carry out training and develop new scientific research, methodologically well elaborated.

Among the complications of COVID-19 listed, respiratory and neurological ones stood out. A Chinese study corroborates this finding, which analyzed 803 medical records of patients infected with COVID-19 and identified the preponderance of respiratory complications, mainly characterized by respiratory failure and pulmonary embolism\(^{(15)}\). The impairment of gas exchange between the lungs and circulating blood, and the intense and rapid hypoxemia caused by COVID-19, are factors that support the severity of the disease\(^{(16}-18,19\)) and justify the increase in mortality due to respiratory complications\(^{(18}-19\)).

This context is also similar to a Spanish study, which reviewed 452 medical records of patients who presented with COVID-19, and identified a high incidence of pulmonary embolism, even with the use of thromboprophylaxis, and even in cases considered not critically ill\(^{(19)}\).

In order to limit the respiratory complication in COVID-19 and reduce the use of ventilatory support and hospitalizations in intensive care units, it is essential to promote knowledge about the early recognition of this condition, the precise treatment, patterns of complications and risk factors, to avoid future, irreversible consequences capable of harming countless lives\(^{(14},15,18-19\))

Regarding neurological complications, an American study carried out with 40,427 participants pointed to encephalopathy and stroke as the most common neurological conditions resulting from COVID-19\(^{(17)}\). It is known that respiratory viral infections have the central nervous system as one of their routes, and this may explain the high incidence of this type of complication\(^{(23)}\).

New pathophysiological neurological changes caused by COVID-19 are to be expected. In the meantime, an evaluation is recommended for patients who test positive for COVID-19 and have underlying neurological disease and for patients who start to present neurological signs and symptoms, such as headache, mental confusion, paresthesia, without disease or any previous neurological changes, in order to avoid future complications, seeking prevention and effective treatment, for a better clinical outcome of patients affected by COVID-19\(^{(16}-17,20,22\))

The scenario composed of the main complications of COVID-19 demonstrates that its consequences go far beyond the acute period of infection, hospitalization, and reinforces the need to invest in strategies to contain the virus, fundamental to reduce deaths, flatten the growth curve and avoid the collapse of the health system\(^{(1)}\).

The complications of COVID-19 instigate reflection and understanding of its future implications for the patient affected by the disease, for society and for the health system. There will possibly be an increase in the number of patients seeking health services after the pandemic period due to the complications arising from the disease or due to the association between complications, such as depressive and cardiac conditions, and this will require a restructuring of the health services, to support the clinical practice\(^{(14,16}-17,18\))

After the pandemic, an exponential increase in elective procedures, in the number of decompensated patients due to non-adherence to treatments, and consequent overload of the health system and public spending are expected. Fear of COVID-19 has led to the postponement of elective procedures, and as a result, there will possibly be an increase in urgent cases while patients are waiting for their procedures\(^{(14,16,24}\).
In addition, due to the fear of going to the hospital and contracting COVID-19, many patients may have ignored important symptoms at home, a factor that exacerbates morbidity and mortality and out-of-hospital cardiorespiratory arrest(14,16,24).

All over the world there are cities, regions and countries completely changing their routines due to the impact caused by COVID-19. The health system has been trying to adapt and control the shortage of basic supplies of personal protective equipment (PPE), diagnostic tests, equipment, and structure-related problems in order to avoid the collapse of the system, minimize extreme overload of health professionals, and meet the increased demand of existing critically ill patients(1). Having knowledge about the current scenario and foreseeing its possible implications allows for an early analysis of existing weaknesses and lessons learned from a pandemic period so as to provide the opportunity for proper health planning and to determine the best clinical practices(1,24).

Despite the variability of studies that address the complications of COVID-19, few publications presented scientific evidence about its implications for the future, which points to the need for reflection and deepening in this area, given the need to understand the possible impacts on the health of the individual affected by this disease in the long term, and also on the health system. In addition to the scarcity of evidence on the possible effects of COVID complications for the future, the adoption of five sources of information is another limitation of the present study, since this amount of databases may not have been sufficient to exhaust the scientific literature on the subject. Another point is the low level of evidence of the manuscripts included in the sample, which makes it difficult to generalize the findings. This evidence is considered less robust and lacking in methodological strategies that include the synthesis of the best scientific evidence, that is, from systematic reviews or randomized clinical trials. It is suggested that the scientific evidence and reflections established here can support the construction and validation of care protocols, capable of guiding the clinical practice and better decision-making, in view of the possible complications of COVID-19 and subsequent impacts.

CONCLUSION

The main complications of COVID-19 are of neurological, respiratory, psychiatric, cardiovascular, nutritional and muscular nature. Respiratory and neurological complications were predominant in the literature. The main future implications resulting from COVID-19 for patients and the health system are the increase in the number of patients seeking health care, greater need to structuring health services, sudden increase in elective procedures, greater number of decompensated patients due to non-adherence to treatments, overloading of the health system, increased public spending, and increased incidence of out-of-hospital cardiac arrest and death.

This study contributes to research, care and teaching in health and nursing by presenting a broad theoretical framework on the complications of COVID-19 and its future implications, in a single study, in order to support a reflection, decision making, before the existing needs and weaknesses.

REFERENCES


