

Anxiety and dyspnea in patients infected with the new coronavirus

Ansiedade e dispneia em pacientes infectados pelo novo coronavírus

La ansiedad y disnea en pacientes infectados con el nuevo coronavirus

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Resumo

Introdução. A COVID-19 tem a dificuldade respiratória como um dos sinais mais comuns. Além disso, devido às múltiplas variáveis envolvidas no manejo da doença, pesquisas mostram o grande impacto na saúde mental da população, principalmente devido à ansiedade. **Objetivo.** Analisar e mensurar a relação entre ansiedade e dispneia em pacientes infectados pelo coronavírus. **Método.** Trata-se de um estudo quantitativo e qualitativo, realizado a partir de uma revisão integrativa nos periódicos indexados nas bases de dados *ScienceDirect*, *PubMed* e *Web of Science*, no período entre 2019 e 2021. A maioria das pesquisas não respondeu à questão de pesquisa na revisão, mostrando apenas ansiedade ou apenas dificuldades respiratórias entre os pacientes com coronavírus. **Resultado.** A literatura mostra uma correlação entre ansiedade e dificuldades respiratórias entre os pacientes infectados pelo coronavírus, mas em uma perspectiva mais qualitativa, apresentando poucos resultados mensuráveis. No estudo de Turan *et al.*, 18,2% dos pacientes com sintomas de ansiedade e que foram infectados pelo novo coronavírus também apresentaram dispneia. **Conclusão.** Existe uma correlação entre os fatores que necessitam de análise mais aprofundada por pesquisas que gerenciem a relação direta entre eles.

Unitermos. Ansiedade; Sars-Cov-2; Dispneia

Abstract

Introduction. COVID-19 which has respiratory difficulty as one of the most common signs. In addition, due to the multiple variables involved in the management of the disease, research shows the great impact on the population's mental health, mainly due to anxiety. **Objective.** To analyze and measure the relationship between anxiety and dyspnea in patients infected with coronavirus. **Method.** This is a quantitative and qualitative study, carried out based on an integrative review in the journals indexed in the ScienceDirect, PubMed and Web of Science databases, in the period between 2019 and 2021. Most research did not answer the research question in the review, showing only anxiety or only breathing difficulties among patients with coronavirus. **Result.** The literature shows a correlation between anxiety and breathing difficulties among patients infected with coronavirus, but in a more qualitative perspective, showing few measurable results. In the study by Turan *et al.*, 18.2% of the patients with symptoms of anxiety and who were infected with the new coronavirus also showed dyspnea.

Conclusion. There is a correlation between the factors that need further analysis by research that manages the direct relationship between them.

Keywords. Anxiety; Sars-Cov-2; Dyspnea

Resumen

Introducción. COVID-19 que tiene dificultad respiratoria como uno de los signos más comunes. Además, debido a las múltiples variables que intervienen en el manejo de la enfermedad, las investigaciones muestran el gran impacto en la salud mental de la población, principalmente por la ansiedad. **Objetivo.** Analizar y medir la relación entre ansiedad y disnea en pacientes infectados por coronavirus. **Método.** Se trata de un estudio cuantitativo y cualitativo, realizado a partir de una revisión integradora en las revistas indexadas en las bases de datos *ScienceDirect*, *PubMed* y *Web of Science*, en el período comprendido entre 2019 y 2021. La mayoría de las investigaciones no respondieron a la pregunta de investigación en la revisión, mostrando solo ansiedad o solo dificultades respiratorias entre los pacientes con coronavirus. **Resultado.** La literatura muestra una correlación entre la ansiedad y las dificultades respiratorias entre los pacientes infectados con coronavirus, pero en una perspectiva más cualitativa, mostrando pocos resultados medibles. En el estudio de Turan *et al.*, el 18,2% de los pacientes con síntomas de ansiedad y que estaban infectados por el nuevo coronavirus también presentaban disnea. **Conclusión.** Existe una correlación entre los factores que necesitan mayor análisis por parte de investigaciones que manejen la relación directa entre ellos.

Palabras clave. Ansiedad; Sars-Cov-2; Disnea

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INTRODUCTION

The new coronavirus, classified as SARS-Cov-2, is a component of the *Coronaviridae* family, was identified in December 2019 in the city of Wuhan, China, giving rise to a new type of pneumonia. The World Health Organization noted the disease currently referred to as COVID-19 and on March 11, 2020, declared a pandemic in view of the international public health emergency. The disease caused by the SARS-CoV-2 virus is identified by symptoms such as fever, dry cough, fatigue, dyspnea, and lymphopenia. Evidenced with 80% similarities in nucleotides of SARS-CoV-1, SARS-Cov-2 is shown to be different in phylogenetic analyses¹.

The epidemiological profile is in continuous evolution; patients in severe cases present respiratory distress, heat shock and sepsis, and are referred for treatment through intensive care and intubation. The virus transmission occurs through large respiratory droplets and due to direct contact with infected secretions. To reduce the risk of transmission, on March 23, 2020, the UK government issued a directive to isolate and socially distance individuals. However, according to the World Health Organization, the measures implemented may result in increased anxiety².

In addition to COVID-19 symptoms, contagious patients may evidence a range of traumatic and stressful episodes, such as the experience of physical/social isolation, fear of death and/or family members. The intensity of symptoms may also be associated with several sociodemographic variables, including age, gender, and social assistance. Thus, the COVID-19 pandemic stands out with negative consequences on both physical and mental health. According to the most recent studies from China, symptoms of anxiety and depression are found in 31.9% and 33.7% of patients infected with the virus³⁻⁵.

Among the predominant mental disorders is anxiety, which is characterized by persistent worry, nervousness, or fear. Studies state that in the United Kingdom, approximately 1 in 10 individuals face some anxiety-related disorder. The literature also highlights that several negative consequences are intertwined with anxiety, including poor quality of life. Individuals positive for COVID-19 diagnosed

with anxiety and depression are possibly subject to have a worsening prognosis and have been found to be prone to acquire harmful impacts².

Anxiety, depression, and somatization cause a multitude of side effects, according to doctors, specifically anxiety can result in somatic/collateral symptoms such as dyspnea, tachycardia, and sweating. Confirmation that anxiety has a bidirectional relationship with hyperventilation is supported by the fact that individuals with idiopathic hyperventilation score higher on anxiety and depression scales⁶.

Dyspnea is defined as a subjective syndrome of respiratory discomfort that varies in intensity and is related to physiological, psychological, environmental, and social factors. Patients who experience worsening of respiratory discomfort may associate shortness of breath as a threat linked to anxiety or depressive symptoms, with secondary physical consequences^{6,7}.

Consequently, dyspnea may be linked to symptoms of anxiety or depression in infected patients during hospitalization. Moreover, dyspnea in patients with COVID-19 may evolve rapidly to acute respiratory failure, so that the use of ventilation is strongly recommended. Such factors highlight the importance of mental health care, so that the psychological dimension is not annulled in this group of patients. The understanding and clarification of the psychological demands of patients with COVID-19 during and after the development of the disease allows broad knowledge

about the current scenario in society and may be the most efficient way to prevent somatic pictures in future crises/pandemics^{8,9}.

Thus, this study aims to synthesize the evidence on the relationship between anxiety and pictures of respiratory distress in coronavirus-infected patients. In addition, we intend to analyze the methods used to manage the situation analyzed and the debate on the subject in the literature.

METHOD

This is a study of quanti-qualitative approach, carried out through an integrative review of publications on the correlation between anxiety and dyspnea caused by the new coronavirus infection. Integrative review is one of the modalities of systematic review, which allows tracing an overview of the literature already published, based on opinions, concepts, or ideas from scientific or empirical research, providing an expanded view on a particular topic¹⁰.

To maintain methodological rigor, this review had six steps: 1) elaboration of the research question; 2) sampling or literature search of primary studies; 3) extraction of data from primary studies; 4) assessment of primary studies included in the review; 5) analysis and synthesis of review results; and 6) presentation of the integrative review¹¹.

The research question: "What is the impact of people who suffer from anxiety and were infected by the new coronavirus on the development of dyspnea pictures?" was elaborated using the PICO strategy, synthesized by the

acronym where "P" corresponds to the population (anxious), "I" to the phenomenon of interest (coronavirus infection) and "Co" to the context of the study (Development of dyspnea pictures)¹².

The search for studies was conducted from May to January 2020 and the following descriptors were used, according to the Descriptors in Health Sciences (DeCS): Anxiety; Coronavirus; Dyspnea. The selected descriptors and keywords were combined according to the search in the ScienceDirect (Elsevier), Science Citation Index Expanded (Web of Science) and PubMed Central databases. To cross-reference the terms, the Boolean logical operator "AND" was used in both databases to obtain the largest possible number of articles that answered the guiding questions. These terms should be present in the title, abstract and subject field.

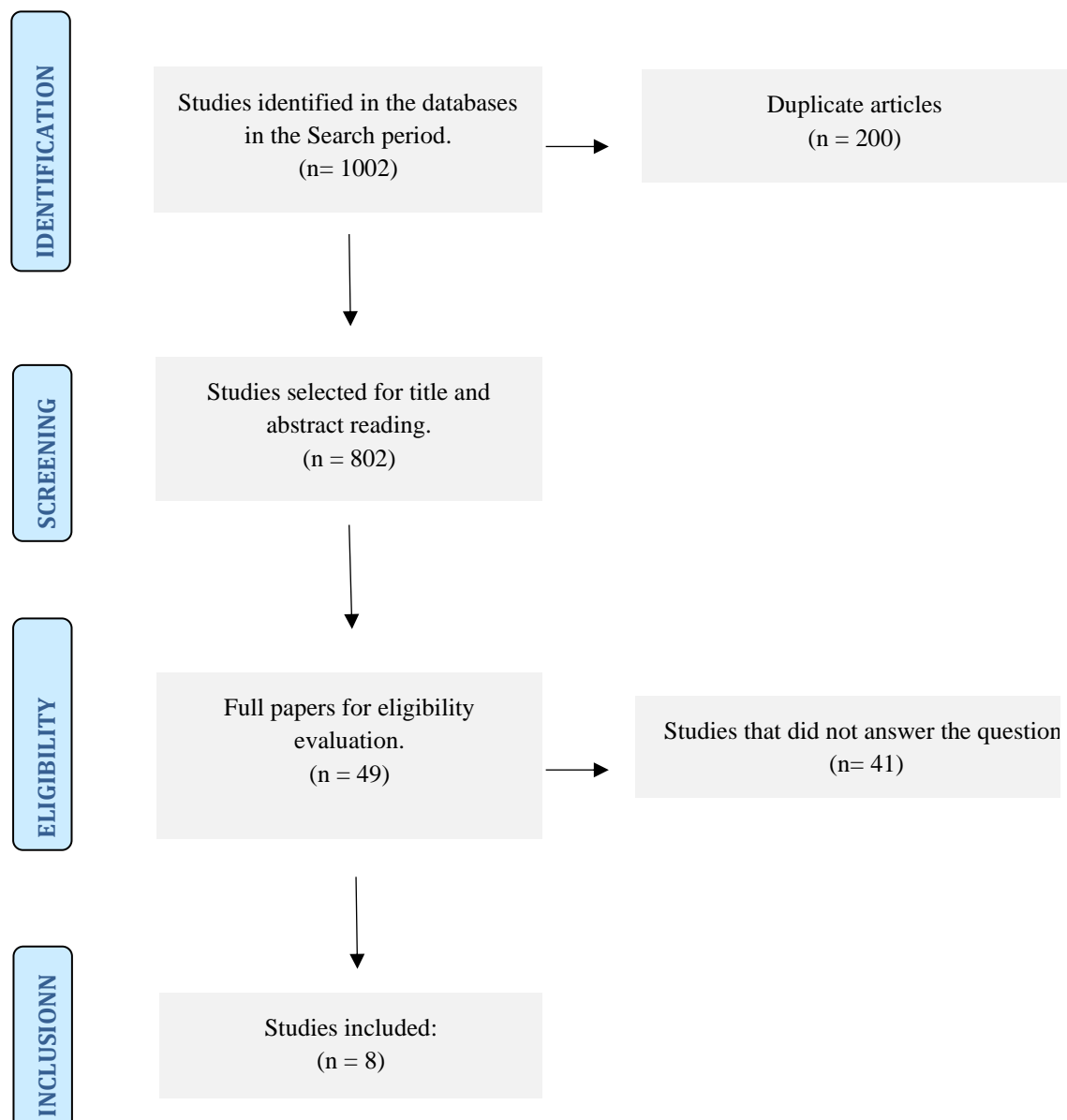
The following inclusion criteria were considered: original articles and literature review articles; articles with abstract and full text available for analysis; articles published in Portuguese between the years 2019 and 2021. Studies, which did not address dyspnea in people suffering from anxiety, or that had descriptors as cross-cutting themes in the study, without meeting the proposed objective, literature reviews, theses, dissertations, reviews, case reports and experience reports were excluded.

In the article selection process, a total of 1002 publications were identified; of these, 802 papers were refined according to the search period for being published in more than one database, leaving X papers; Z were excluded

for not meeting the theme, being pre-selected W articles. Of the pre-selected studies, A for not answering the research question. Finally, Y articles were selected for the final sample

In the next step, the 7 selected studies were analyzed, and the relevant information was summarized. From this, concepts were extracted and grouped by similarity of content. The following flowchart reflects this information.

Fluxogram 1. Article Selection Process for the Literature Review.



RESULTS AND DISCUSSION

In the search for articles, 49 papers were selected from the literature that mentioned anxiety and dyspnea during the pandemic caused by the new coronavirus. However, there was a higher concentration of research on uncorrelated themes, citing only the prevalence of anxiety or only dyspnea. After filtering the eligibility criteria that addressed the proposed issue, 8 studies remained to be analyzed in detail. The Table 1 reflects what each author intended, and the results obtained by them.

Mental health has become one of the main complications during the pandemic caused by Sars-Cov-2, which can often alter the prognosis of infected patients. Moreover, the disease developed by the virus is marked by a picture of dyspnea that constantly evolves with severity, consequently some studies show that about 60% of patients require some intervention by oxygen and about 20% require Intensive Care Unit (ICU)^{7,13}.

In other crises involving pathogens of the same origin as the new coronavirus, such as Sars-Cov-1 or Mers-Cov-1, a systematic review showed that anxiety (35.7%) was one of the most frequent symptoms in patients admitted to hospitals with these viruses¹⁴. Moreover, it was also found that these symptoms were persistent even after 6 months of infection and up to 3 years in 40% of survivors^{9,15}.

Table 1. Layout of the studies used in the review.

Authors/Year	Title	Country	Final Sample (n)	Anxiety scale	Results
Shangguan <i>et al.</i> (2020) ¹³	Prevalence and correlates of somatization in anxious individuals in a Chinese online crisis intervention during COVID-19 epidemic	China	Total: 1.134 Women: 797 Men: 337	Generalized Anxiety Disorder-7 (GAD-7)	Breathlessness and Weakness were symptoms similar to the clinical manifestations of COVID-19, which may increase anxiety or fear. Prevalence of dyspnea was 3.1%, much higher than in the previous survey (0.4%).
Poyraz <i>et al.</i> (2021) ¹⁶	Psychiatric morbidity and protracted symptoms after COVID-19	Turkey	Total: 284 Women: 139 Men: 140	Hospital Anxiety and Depression Scale (HADS)	About 33% of patients infected with COVID-19 manifested anxiety within 50 days of diagnosis. 20.8% of the analyzed patients had saturation lower than 94 and 21.2% required oxygen during hospitalization.
Turan <i>et al.</i> (2021) ¹⁴	Characteristics and outcomes of COVID-19 inpatients who underwent psychiatric consultations	Turkey	Total: 892 Women: - Men: 412	International Statistical Classification of Diseases and Related Health Problems, 10th revision (ICD-10),	61.8% of all psychiatric patients were classified as having anxiety disorders. Of these, 18.2% presented with dyspnea. The author correlates greater need for oxygen due to stress, intubation rate, longer hospital stay when compared to other patients, and use of psychiatric drugs.
Kong <i>et al.</i> (2020) ¹⁷	Prevalence and Factors Associated with Depression and Anxiety of Hospitalized Patients with COVID-19	China	Total: 144 Women: 74 Men: 70	Hospital Anxiety and Depression Scale (HADS)	Anxiety was present among 34.72% of patients, 17.36% were mild, 12.5% were medium and 4.86% were severe. In the study, low oxygen saturation was present among 11.11% of patients. The quantitative correlation between anxiety and oxygen saturation was positive ($\beta=-2.140$, $p=0.049$).
Mina <i>et al.</i> (2020) ⁵	An online observational study assessing clinical characteristics and impacts of the COVID-19 pandemic on mental health: a perspective study from Bangladesh	Bangladesh	Total: 153 Women: 43 Men: 110	Generalized Anxiety Disorder 7-item (GAD-7)	63.5% of patients presented anxiety. Of these, 22.8% and 18.5% were severe and medium cases, respectively. Dyspnea was identified in 23.5% of patients.
Li <i>et al.</i> (2020) ⁷	The Associated Factors of Anxiety and Depressive Symptoms in COVID-19 Patients Hospitalized in Wuhan, China	China	Total: 99 Women: 45 Men: 54	Hospital Anxiety and Depression Scale (HADS)	The mean research score for anxiety was 6.69. Regarding anxiety, 26.31% (n=26) were borderline cases and 15.2% (n=15) were abnormal. For dyspnea, 31.3% presented during the walk.
Wang <i>et al.</i> (2020) ¹⁸	Immediate Psychological Responses and Associated Factors during the Initial Stage of the 2019 Coronavirus Disease (COVID-19) Epidemic among the General Population in China	China	Total: 1.210 Women: 814 Men: 396	Impact of Event Scale-Revised (IES-R) / Depression, Anxiety and Stress Scale (DASS-21)	In this study 36.3% of participants were identified with anxiety disorders. Of these, 7.5% were mild, 20.4% were medium and 8.4% were severe. Only 0.4% of patients presented some respiratory difficulty.

In this new lineage of the *Coronaviridae* family, research has already shown that psychological symptoms are being identified even 50 days after the initial diagnosis¹⁹. During the worldwide spread of the pandemic in 2020, an absurd increase of new patients diagnosed with anxiety disorders (+40%) was observed in Germany in March, which marked the beginning of lockdown in the country⁴.

Among anxiety disorders, for example panic disorder, factors such as mild hyperventilation and other abnormal parameters in breathing are highlighted. There are complex correlations between respiratory, organic, physiological, and psychiatric disorders in hyperventilation. In patients who are unaware of the consequences of excessive ventilation, stress hyperventilation causes signs that are generally interpreted as a risk factor. This misinterpretation of symptoms results in increased fear and acts on the autonomic nervous system, causing an increase in respiratory rate, generating a high CO₂ reduction and elevating hypocapnics. Such actions drive positive feedback, amplifying the panic reaction and forming a panic attack.

In the study by Li 2020⁷, reported that 34.72% of patients infected with COVID-19 demonstrated anxiety, through the Hospital Anxiety and Depression Scale (HADS), which was the most prevalent among the selected studies. This consists of two subscales, which are rated separately. One scale measures anxiety and the other depression, with seven items each. The items are answered using a four-point ordinal scale (0-nonexistent, 3-very severe). All items that

presented associations simultaneously with physical disturbance were intentionally excluded by the authors of the scale. The examples of physical disorders were vegetative symptoms such as headaches, insomnia, and fatigue. Only psychic symptoms are bases for the excluded items in the scale. Only HADS attends, at least partially, the main impasse reported by most authors of anxiety and depression assessment: Physical disorders of individuals have influence on the results of the scales²⁰.

In recent years, various scales have been implemented with proposals to evaluate dyspnea. However, it is necessary to understand the concepts between current and usual dyspnea. During or after a run it is common to have the symptom as a characteristic of the precise moment, this fact defines current dyspnea. The usual dyspnea is characterized by symptoms of limitations evidenced in the execution of daily activities, such as climbing stairs. In the study by Li 2020⁷, the authors used the Modified Medical Research Council (mMRC) scale, which includes five degrees of graduation, ranging from 0 for no respiratory difficulty, except in strenuous exercises, up to 4 when the patient feels very short of breath in daily activities such as dressing or bathing. The authors point out that dyspnea is intrinsically interconnected with psychological events, thus breathlessness by hospitalized patients may be associated with anxiety as a secondary response²¹.

In addition, some conditions may be used or mediated in the design of dyspnea. Triggering conditions: Occupational

and environmental displays, exertional conditions, climatic variation, changes in mood etc. Comparison: Feeling of exhaustion, effort, fatigue, suffocation, chest distress, etc. Number of attacks and periodicity. Intensity: it is evaluated through specific scales and factors which are related to quality of life. Aspects that are interconnected: Edema, cough, palpitations, among others. Factors for improvement: Category of medication, rest, positions the patient is in, especially in decubitus²¹.

The pathophysiology that relates anxiety and dyspnea in patients with COVID-19 is marked by the "cytokine storm" of the infection, which produces an effect both on the respiratory system of the individual and on the nervous system. The cytokines that reach the brain influence the synthesis, release, and reuptake of neurotransmitters, such as dopamine, serotonin, norepinephrine, and monoamines, some of which are directly linked to anxiety disorders²². In Turan 2021¹⁴, the authors measured that 18.2% of patients, infected by COVID-19 and who were identified by some anxiety disorder, presented pictures of need for mechanical ventilation and high rates of intubation to supply oxygen. The authors also highlight the stress triggered by the infection, and, also the fact that patients with anxiety disorders remain hospitalized for a longer period of time compared to other patients without this psychiatric disorder as reasons for the development of the situation¹⁵.

In the literature, some other aspects are also highlighted as impacting on the mental health of the patient,

among them social isolation with limited social support, high exposure to negative media information about the pandemic and at the same time the lack of concrete information to the layperson about the consequences of the disease. In addition, factors such as stigma, public concern, health system overload and personal aspects such as financial situation and home environment can exacerbate psychiatric symptoms^{2,7}.

In Shangguan 2020¹³, the authors reinforce the idea that dyspnea is multidimensional, not just physiological. To this end, they demonstrated previous studies evoking that breathlessness is more present in patients with anxiety, finding in other work that 9 to 13% of residents in a community have mild to moderate dyspnea. This more retrospective fact is also demonstrated in the research of Li 2020⁷, analyzing patients with chronic obstructive pulmonary disease (COPD) the authors evidenced that anxiety causes a cycle of hyperventilation, the opposite is also true. However, when they analyzed the relationship of patients with COVID-19 they did not assess a positive relationship between dyspnea and anxiety, reporting that one of the reasons for the result could have been the small sample used⁷.

In a survey, the authors portrayed that 38% of patients who were in the ICU reported anxiety symptoms²³. However, a striking aspect in the literature is the development of nocebo effect of anxiety, through side effects such as dyspnea, tachycardia, and sweating, are very common in randomized clinical trials⁶.

Some strategies are found in the literature for the management of the situation of breathing difficulties in line with anxiety. The clinical recovery time of anxiety is marked from psychological intervention to improvement in fever symptoms, oxygen saturation and respiratory rate for at least 72 hours, and may be a differential in increasing confidence and decreasing fear and discomfort of the patient. Respiratory physiotherapy was one of the hypotheses raised, although there are still no concrete scientific results on its efficiency during the acute phase^{8,24-26}.

Literature findings on the relationship between anxiety and dyspnea in patients infected with Sars-Cov-2 are still scarce. Even the selected papers show little data between the two variables, being characterized as one of the difficulties of this review. Other findings are also associated in relation to anxiety in patients with COVID-19, one of the most common being symptoms of depression, often analyzed together and considered as correlated, one aggravating the other. Alcohol consumption was a factor evidenced as aggravating the latter two disorders, and an increase in hazardous consumption of 29.1% was identified during the pandemic period. Another association in the analysis was fatigue, reported among 27% of patients with some symptom of anxiety or depression and which was often classified as chronic, being present in 87.4% of patients for 60 days according to some studies^{3,25-28}.

CONCLUSION

We conclude that there was a greater development of respiratory distress in patients infected with the new coronavirus who also presented criteria for anxiety classification. The most used scale to diagnose anxiety and dyspnea in patients were, respectively, the Hospital Anxiety and Depression Scale (HADS) and the Modified Medical Research Council (mMRC), although the latter is less cited than the former and other more subjective or less measurable criteria, such as oxygen saturation and respiratory rate, are used as instruments. There are many works in literature that surround the descriptors of the theme, although most do not answer the question of this research, which seeks to make the correlation between the two criteria in infected patients and can be seen as a limiting factor of this work.

Thus, the present study opens spaces for new attributions to scientific research by instigating debate, consolidating data and correlations on the theme. Original research that manages exactly the research question worked out in this review may contribute with other new review analyses in order to establish strategies for patient care, since there are few intensive care that work on the two biases as it was highlighted throughout the study.

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