

Original Article

## Follow Up in Patients with Respiratory Disability after ARDS Related to Covid-19: A Systematic Review

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### Abstract

**Introduction:** Acute Respiratory Distress Syndrome (ARDS) is an acute inflammatory pulmonary process that leads to protein-rich, non-hydrostatic pulmonary edema, undesirable hypoxemia and lung stiffness. Due to Covid - 19 a significant proportion of people who will require hospitalization to treat Covid-19, between 15%-30%, will develop severe respiratory failure, ARDS and an increased likelihood of intubation for mechanical respiratory support.

**Aim:**The aim of this study was to investigate the pulmonary function in COVID-19 related ARDS survivors after hospitalization.

**Methods:** A search was performed at the Greek and international literature, as well at the online Databases PubMed, Cochrane, Embase, Google Scholar. Exclusion and integration criteria were set for the studies found and a flow chart was created for the studies included

**Results:**Through the search, 103 articles were found matching the subject under study and after further evaluation, 4 articles were included. The majority of the articles highlight that after ARDS occurs due to COVID-19, patients face impaired pulmonary function in combination with other physical and psychological symptoms like weakness, anxiety, depression and generalized functional disability.

**Conclusions:**It is a fact that COVID-19 disease, in severe form and following the need for hospitalization due to the development of ARDS, results in an increased likelihood of prolonged occurrence of some symptoms of impaired respiratory function. Impaired CO<sub>2</sub> diffusion is observed in the majority of studies as well as impaired respiratory function regarding prolonged imaging findings and impaired physical function.

**Key words:** ARDS, SARS-CoV-2, ICU, Follow Up, Pulmonary function.

## Introduction

Acute Respiratory Distress Syndrome (ARDS) is a condition with multiple risk factors, resulting in acute respiratory failure and appears in various severity statuses. Very often ARDS can lead to ICU hospitalization with a high mortality rate. Most cohort studies suggest a pattern of clinical risk factors with pneumonia being the major risk factor (35-50%) followed by pulmonary sepsis (30%), aspiration (10%) and trauma (10%) (Atzrodt CL et al., 2020). The new coronavirus emerged in China in early 2020 and was added in the causes that can lead to severe ARDS. A significant fraction of people who will require hospitalization to treat Covid-19, between 15%-30%, will develop severe respiratory failure, ARDS and an increased likelihood of intubation for mechanical respiratory support. (Seyed Hosseini E et al., 2020). It is a fact that COVID-19 disease, in severe form and following the need for hospitalization due to the development of ARDS, results in an increased likelihood of prolonged occurrence of some symptoms, especially of impaired respiratory function (Attaway A H et al., 2021).

According to the epidemiological data on the disease, there is a dramatic variability in the incidence of the disease between different continents. In particular, in Europe the incidence of the disease is 17,9/100 000 person-years and in the USA 78,9/100 000 person-years, with relative geographical variability (Rezoagli et al., 2017). These rates are derived from surveys based on hospitalization of patients in whom ARDS incidence ranged from 7.1% to 12.5% of the total incidence of all ICU cases in Europe (Pham et al., 2017). Regarding ARDS due to Covid - 19, the majority of the articles highlight that after ARDS, patients face impaired pulmonary function in combination with other physical and psychological symptoms like weakness, anxiety, depression and generalized functional disability (Fanelli et al., 2013). Thus, radiological and physiological abnormalities were still found in a considerable proportion of COVID-19 survivors without critical cases 3 months after discharge, impaired diffusing capacity for carbon monoxide (prevalence 27%), and reduced exercise capacity mean 6-min

walking distance (Torres-Castro R et al., 2020).

The majority of the studies focused on the relationship between the clinical characteristics and the pulmonary function in order to determine long-term clinical outcomes in survivors of severe acute respiratory syndrome (SARS) after hospitalization or intensive care unit admission (Zhao YM et al., 2020). They evaluated health-related quality of life (HRQoL) and physical and psychological impairments in ARDS survivors from 3 months to 5 years follow-up after ICU discharge. The tools that were mostly used included Computed Tomography (CT), the 6 minute-walk test, quality of life assessment questionnaires and respiratory parameters assessment (dynamic vital capacity [FVC], fast expiratory volume of air in one-minute [FEV1], FEV1/FVC ratio, total lung capacity [TLC], residual capacity [RV], vital capacity [VC]) (Ahmed H et al., 2020).

This systematic review aimed to investigate the pulmonary function in ARDS survivors due to Covid - 19 disease after ICU hospitalization.

## Methods

We collected data from the international electronic scientific bases PubMed, SCOPUS, EMBASE as well as at the Greek IATROTEK both in English and Greek language respectively. Regarding the searching strategy, the following keyword were used: "ARDS", "SARS-CoV-2", "ICU", "COVID-19", "Follow up", "Pulmonary function". No limitations were applied regarding the articles' publication time. International or local locations of survey appliances were included. This systematic review included studies that met the following criteria:

- Studies were conducted on adult humans.
- Studies focused on ARDS related to Covid - 19.
- Studies were published in Greek or English. Moreover, the literature exclusion criteria were the followings:
- Studies were case studies, editorials, and letters to the editor
- Studies were not in English and Greek language.
- Studies were conducted on animals.
- Patients were not hospitalized in the ICU.

The following data were extracted from each study after the selection of the studies included in the systematic review: first author's name, the country of origin of the study, the publication year, the type of study, the purpose of the study, the sample studied, the respiratory related findings.

## Results

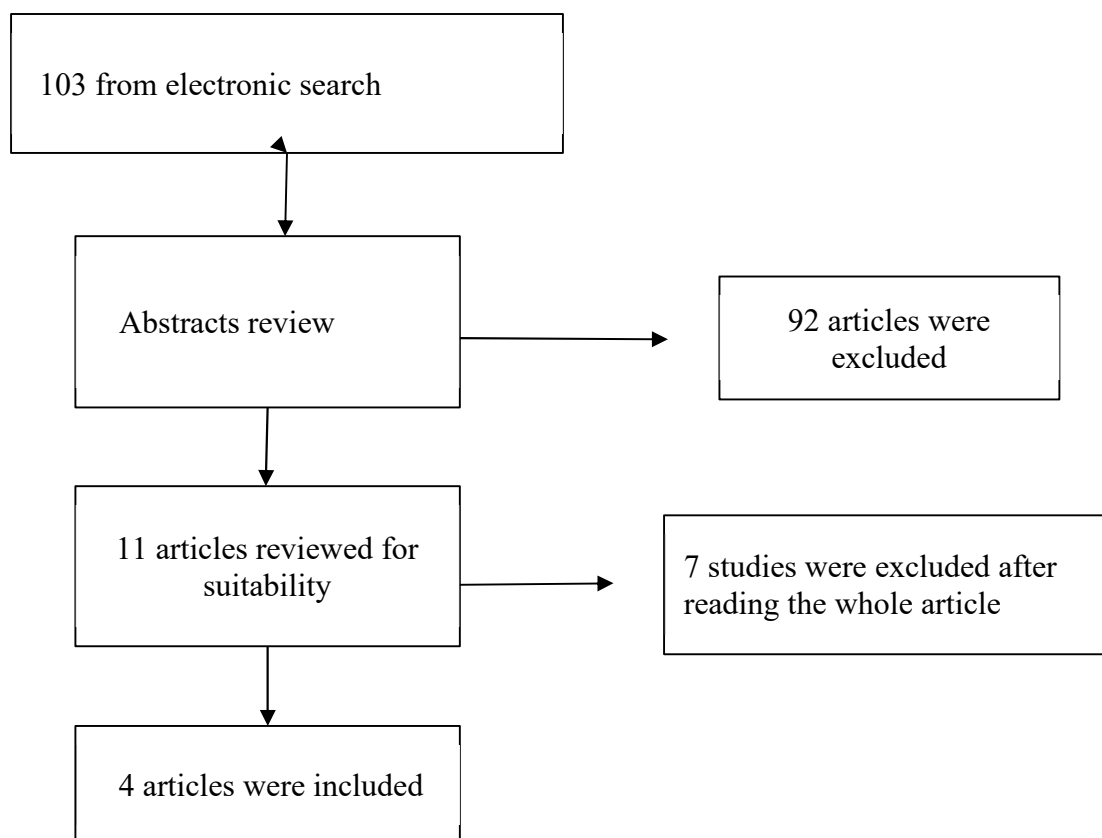
There were 103 articles reviewed, of which 92 were rejected due to a non-relevant title or abstract. In the end, based on the inclusion and exclusion criteria, four studies were included in this systematic review after reading the full text of 11 articles (Figure I). A summary of the study characteristics is presented in Table I. Almost all of the studies were conducted in the European continent, specifically, one in France, one in Spain, one in Italy and one in collaboration between Italy and Canada. In terms of study design, all of the studies were

prospective.

### ***Main results regarding respiratory function after ICU hospitalization due to COVID - 19 related ARDS.***

According to our systematic review results as shown on Table I, the main aims of the studies were the investigation of the long-term physical, functional and mental status, the long-term mortality, quality of life, functional and psychological recovery of the patients, as well as computed tomography (CT) characteristics. The dominant respiratory findings include dyspnoea (from 28,5% to 68.5% of the studied population) in the majority of the studies, followed by CT abnormal findings and reduced lung diffusing capacity. It's important to highlight that among the four studies, two performed the follow up on the first year after discharge, one after 2 months and one after 3 months.

**Figure I. Flow chart of the systematic review**



**Table I. Summary of the studies in the systematic review**

First author, Study design, Country	Purpose of the study	Study sample	Main respiratory findings
Raphael Laurent et al, prospective study, France, 2023	To describe the long-term physical, functional and mental status of COVID-19 intensive care unit (ICU) patients and their family members 1 year after ICU discharge.	n=54 patients	Dyspnea= 68,5% CT abnormal findings= 72,3%
Alberto Zangrillo et al, Prospective observational study, Italy, 2022	To investigate long term mortality, quality of life, functional and psychological recovery of the patients, as well as computed tomography (CT) characteristics of the lungs 1 year after ICU discharge.	n= 61 patients	Exertional dyspnea= 28,5% CT abnormal findings= 13,8% median residual lung damage=7,6%
Jessica González et al, Prospective Cohort, Spain, 2021	To investigate the long-term pulmonary sequelae in critical patients who survive COVID-19	n= 62 patients	Dyspnea =46.7% Cough =34.4% Lung diffusing capacity <80% = 82% Abnormal CT findings= 70.2%
Giacomo Monti et al, prospective follow-up study, Italy, 2021	To assess the quality of life of invasively ventilated COVID-19 ARDS survivors 2 months after discharge	n=39 patients	Excessional dyspnea= 51%

## Discussion

In this systematic review, we aimed to investigate the respiratory function in ARDS survivors due to Covid - 19 disease after ICU hospitalization. It was an attempt to gather the latest scientific findings regarding the above-mentioned aim three years after the pandemic broke out.

Experience so far with previous respiratory viruses and ARDS in general shows that patients experience respiratory problems for a long time after hospital discharge. Accordingly, some studies describe prolonged illness from Covid-19 in terms of

persistence of respiratory symptoms. In addition to the above studies, it is evident that Covid-19 affects respiratory functionality at different levels and severity. Furthermore, according to other systematic reviews, it is a fact that COVID-19 disease, in severe form and following the need for hospitalization due to the development of ARDS, results in an increased likelihood of prolonged occurrence of some symptoms of impaired respiratory function. Impaired CO<sub>2</sub> diffusion is observed in the majority of studies as well as impaired respiratory function in terms of fitness and reduced endurance. Furthermore, the prolonged imaging findings possibly combine

with the above research data without however, a long-term and more massive follow-up. In addition, lower intensity physical symptoms such as effort dyspnea, fatigue and pain are observed in the post-hospitalization period.

The above-mentioned findings from other international systematic reviews, are competitive with this study's findings. The grand majority of the patients face dyspnea after hospital discharge from 2 months to 1 year later. Furthermore, CT scan abnormalities accompany the follow up's findings, up to 72,3% of the studied population. In addition, reduced Lung diffusing capacity and other lung damages are also included in respiratory disabilities.

Both in the 4 studies included (Table 1.) and the other studies compared, similarities were found regarding the assessment tools. Looking further into the respiratory status, the patient's physical condition was studied in terms of endurance and functionality, using the 6-min-walking test in combination with spirometry and other similar tests and in terms of imaging, CT scan was widely used. In addition, regarding the general quality of life assessment, scales such as SF-36 score, Hads scale, EQ5D scale and Post Traumatic Stress Disorder Scale were used.

This systematic review has several limitations that should be mentioned. It's important to highlight that there were no significant findings published from Asian and Latin American countries, which creates barriers to reach a more scientifically documented result. Furthermore, among the included studies, only two had the same follow up period, raising concerns about the possible outcomes of the other two studies that had significantly earlier follow up periods. Although the majority of the scientific community focused on the treatment of COVID-19, yet the scientific evidence for the long-term consequences is really poor. Following the mentioned limitations, the need for further follow up of this survivors' category in a bigger scale and duration, is still present.

**Conclusion:** It is a fact that COVID-19 disease can lead to severe ARDS, most possibly followed by the need for mechanical ventilation in the ICU. The majority of the already existing studies witness various

respiratory related consequences even one year after ICU discharge. Dyspnea is the leading finding followed by prolonged imaging findings, and reduced physical endurance. In addition, lower intensity physical symptoms such as fatigue and pain are observed in the post-hospitalization period. The evolution of symptoms and the general respiratory function of the patient continues to be a major research topic, especially over a five-year period, in order to draw more valid results and conclusions.

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