Comorbidities, COPD and COVID 19

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Abstract

English:

Coronavirus disease 2019 caused by the severe acute respiratory syndrome coronavirus 2 is one of the most pressing health care concerns in 2020. The continually growing number of new cases, the global outspread of the virus and the severity of the disease determined the World Health Organization to declare the outbreak a pandemic.

Twenty per cent of the patients present severe and critical forms that frequently require oxygen supplementation and intensive care unit admission. That is why, to provide optimal care, it is imperative to identify at-risk patients.

Patients with associated chronic diseases are more prone to develop severe and critical forms of the infection. Although the chronic pulmonary obstructive disease is present only in a limited number of coronavirus disease 2019 patients, it is most commonly associated with lung disease and a poor outcome than other comorbidities.

Keywords

COVID-19 • COPD • comorbidities

Impactul comorbidităților asupra pacienților diagnosticați cu BPOC și COVID 19

Rezumat

Romanian:

Boala Coronavirus 2019 cauzată de noua tulpină de coronavirus (SARS-COV-2) este una dintre cele mai presante probleme de sănătate publică ale anului 2020. Numărul de cazuri noi în continuă creștere, extinderea globală a virusului și severitatea bolii au determinat Organizația Mondială a Sănătății să declare boala o pandemie.

20% dintre pacienți prezintă forme severe și critice care necesită frecvent suplimentarea oxigenului și internarea în unități de terapie intensivă. De aceea, pentru a oferi îngrijiri optime, este necesar să se identifice pacienții cu risc.

Pacienții cu boli cronice asociate sunt mai predispuși să dezvolte forme severe și critice ale infecției. Deși boala obstructivă pulmonară cronică este prezentă doar la un număr limitat de pacienți diagnosticați cu boala Coronavirus 2019, este cea mai frecventă boală pulmonară asociată și este comorbiditatea cel mai frecvent asociată cu o evoluție nefavorabilă.

Cuvinte-cheie

COVID 19 • BPOC • comorbidități

Abbreviations

WHO	– World Health Organization
SARS-COV-2	– severe acute respiratory syndrome coronavirus 2
COVID-19	– coronavirus disease 2019
ICU	– intensive care unit
COPD	– chronic obstructive pulmonary disease
ACE-2	– angiotensin-converting enzyme 2

On 31 December 2019, China reported the World Health Organization (WHO) a cluster of patients with pneumonia caused by an unknown virus. On 12 March 2020 the genetic sequence of the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) responsible for the disease called coronavirus disease 2019 (COVID-19) became public, and on 11 March 2020 WHO declared the outbreak a pandemic. The constantly growing number of

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new cases, the global outspread of the virus, the severity of the disease and the lack of an effective response were all arguments in making the decision (1).

At present, the disease affects more than 200 countries, with more than 50,000 new cases reported every day and more than 290,000 reported deaths (1). The rapid outspread of the disease and the significant mortality rate make it necessary to focus on identifying at-risk patients.

There are a few particularities of this disease worth mentioning in regards to the topic.

COVID-19 is a polymorphous infectious disease caused by SARS-COV-2. Most of the patients develop mild forms of the disease (81%) (2), some of whom are fairly asymptomatic (with a ratio of 41.6%) (3). In these cases, radiological images may be inconsistent with pneumonia or may indicate lung infiltrates with limited extension. In comparison, the severe and critical forms represent approximately 19% and more frequently associate with respiratory failure, intensive care unit (ICU) admission, septic shock and death (2).

The positive diagnosis of COVID-19 entails a positive viral nucleic acid test. Since this type of testing is mostly limited, a diagnosis based on epidemiological, clinical and radiological criteria is also accepted. COVID-19 mainly affects patients in the age group of 30–79 years, with only a few patients in the age groups of 0–29 years (10%) and >79 years (3%) (2). Regarding sex distribution, most of the studies describe men as more frequently affected by the disease (4–6). On admission, the patients may present fever (83%–98.6%) (4–6) cough (59.4%–82%) (4–7), fatigue (44%–69.6%) (4–7), anorexia, myalgia, dyspnoea, diarrhoea, dizziness, headache and nausea (4).

Since the disease is highly contagious in the absence of an effective set of preventive measures, we would most likely be facing a large number of severe and even critical cases. Providing optimal care to these patients may become a major challenge as they require especially dedicated personnel, oxygen supplementation and, not seldom, admission to the ICU and ventilator support. Reports show that 15%–20% of the patients diagnosed with COVID-19 need at least a form of oxygen supplementation during the hospital stay (7).

Some patients are more predisposed to develop a severe or critical form than others. Recent studies proved that age, smoking status, associated comorbidities, secondary infections and elevated serum inflammatory parameters are risk factors for developing a severe form of COVID-19 (6–8). Moreover, patients with at least two comorbidities have a higher risk of requiring intensive care admission, invasive ventilation and associated higher mortality rates as opposed to those with only one associated disease (6).

In this context, it is essential to assess which are the most frequently described comorbidities in patients diagnosed with

COVID-19 and whether they have a different impact on the evolution of the disease.

In some studies, hypertension (OR: 2.29, $P < 0.001$), diabetes (OR: 2.47, $P < 0.001$), chronic obstructive pulmonary disease (COPD) (OR: 5.97, $P < 0.001$), cardiovascular disease (OR: 2.93, $P < 0.001$) and cerebrovascular disease (OR: 3.89, $P = 0.002$) were independent risk factors associated with COVID-19 patients (9).

Generally, the comorbidities were reported based on patients' statements making it possible to underestimate certain diseases. Commonly described associated pathologies are hypertension (15%–31%) (4–7, 10–12), cardiovascular diseases (8.4%–53.7%) (4–7, 10), diabetes (9.75%–20%) (4–7, 10, 11, 13), malignancy (1%–7.2%) (4–6), cerebrovascular diseases (1.9%–5.1%) (4, 6), COPD (0.95%–3.2%) (5, 6, 10, 13), chronic kidney disease (1.4%–2.9%) (5, 6, 12) and immunological diseases (1%–4%) (4–6, 12–14).

Wei-Jie G et al. published a study that describes comorbidities in patients with COVID-19 and their impact on outcomes. The need for invasive ventilation or admission to ICU and death are expressions of a poor outcome. The study included 1,590 patients, of whom 25.1% reported having one comorbidity, and 8.2% reported having multiple comorbidities. COPD, chronic kidney disease, cerebrovascular diseases, immunodeficiency, hepatitis B, hypertension, cardiovascular diseases and malignancy are more common in patients with severe COVID-19 than patients with non-severe COVID-19 (6). Moreover, COPD is associated with the highest risk in terms of the need for invasive ventilation and mortality. Out of the patients with COVID-19 and COPD, 50% is associated with a poor outcome, two times more than those with COVID-19 and diabetes. Furthermore, 29.2% of patients require admission to ICU and 20.8% need invasive ventilation, and the mortality rate is 25% (6). At the same time, data from multiple individual studies did not prove an association between COPD and severe forms of COVID-19. The small prevalence of COPD in COVID-19 patients may explain the discrepancy. A meta-analysis that pooled the data from the same studies concluded that a COPD patient has more than five times higher risk of developing a severe form of COVID-19 (15).

There are several reasons why COPD patients may develop severe forms of COVID-19.

First, some studies identify the pulmonary endothelium's angiotensin-converting enzyme 2 (ACE-2) receptor as the primary gateway for the virus. After analysing samples obtained through bronchoscopic techniques, Leung et al. concluded that smokers and patients suffering from COPD present a higher expression of the ACE-2 gene, possibly making them more susceptible to the disease. The same mechanism applies to smokers (8).

Second, patients with COPD are 16 times more likely to develop pneumonia (16). Multiple factors, such as chronic

bronchitis, persistent mucus production, microbiome imbalances, inflammation, impaired host immunity and structural damage, may explain the increased risk of developing pneumonia in COPD patients. Besides being more susceptible to pneumonia, COPD patients require more extended hospital stays and exhibit higher ICU admission rates, when diagnosed with pneumonia (17) in general and may also apply to SARS-COV-2 infection.

As many of the COVID-19 patients have multiple comorbidities, the relationship between them is of great importance.

In general, COPD patients have significantly more associated diseases than non-COPD patients (18). Among patients with moderate to severe COPD, 99.75% reported having one comorbidity, while over half of them, i.e. 55.5%, have four or more associated diseases (19).

Divo et al. described, using lines and knots, the interconnections between the comorbidities of COPD patients and revealed them to be frequent and multiple. The study proves that in the case of COPD patients, coronary artery disease, congestive heart failure, atrial fibrillation, flutter, anxiety and diabetes significantly influence mortality, while systemic hypertension and coronary artery disease influence the patients' response to pulmonary rehabilitation (18).

Recently, there has been a tendency to organise associated diseases into clusters, hoping to evaluate their prognostic value and to facilitate managing these patients. Usually, studies sort comorbidities using five clusters. The first one includes patients with fewer comorbidities. The second one, the cluster of cardiovascular diseases, includes patients diagnosed with hypertension and atherosclerosis. Cachectic patients, who usually suffer from chronic renal diseases and osteoporosis, constitute the third cluster. The metabolic disease cluster includes patients with multiple comorbidities, often diagnosed with obesity, dyslipidaemia, diabetes and hypertension. Last, but of great importance, is the fifth cluster that defines psychological impairment. Patients included in this cluster may suffer from anxiety and depression (19).

Studies published on the same topic used other sorting strategies. Some studies describe the same number of clusters but sort the diseases differently. Raherison et al. established among the five clusters, one for patients with COPD and bronchiectasis (20). Others define only three clusters. All aim to find the most relevant formula for arranging comorbidities to predict better the outcome, hospitalisation lengths, costs, the necessity of invasive ventilation and the best treatment courses.

When treating a COVID-19 patient with COPD, especially one with moderate to severe COPD, it is crucial to consider that it is highly likely that the patient has at least one other disease and thus presents an increased risk for a poor outcome.

While COPD is associated with numerous comorbidities, it is also prevalent in patients suffering from other diseases.

Although insufficiently studied, it seems that patients suffering from other illnesses may also have COPD. COPD is present in 5.9% of patients suffering from an acute coronary syndrome, making them more susceptible to heart failure (21), and in 26%–29% of the patients who have atherosclerosis (21, 22). More than exposure to higher than normal glycaemic serum levels may lead in time to a diminution in lung function, making the association diabetes–COPD probable (23).

Although prospective studies are still necessary, it is fair to say that probably some of the patients diagnosed with COVID-19 that have underlying conditions might also be undiagnosed COPD patients.

Concerning therapy, it seems that these COPD patients could benefit from quarantine. The adherence to controller therapy increased between January and March 2020 with 14.5% (24) reflecting probably the patients' concern and the increased motivation of asthma and COPD patients. There is a post-COVID recommendation for COPD survivors described by Celli and Fabbri (25). They proposed a management plan that pays special attention to the prompt recognition of cardiovascular complications, especially in 30 days following the resolution of the acute phase of the event. It is another modality to avoid the deaths of survivors after pneumonia from a relatively preventable consequence. Smoking cessation for COPD remains another important recommendation. The chronically increased ACE-2 gene expression in airways of current smokers (but not former smokers) and patients with COPD, predisposes individuals to increased risk of coronavirus infections. (8). For the other main therapeutic medications, the Global Initiative for Chronic Obstructive Lung Disease (26) recommends not to avoid inhaled (or oral) corticosteroids, during COVID-19 epidemic, to maintain their regular use and also to provide oxygen therapy if needed (following standard recommendations).

Conclusions

COPD patients remain a fragile and at-risk cohort of patients. The fragility is induced by multiple risk factors such as smoking and pollution, and also by cumulative number of comorbidities and age of this sample of patients.

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