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Short Communication

C-ARDS, a Quick Approach

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Acute Respiratory Distress Syndrome (ARDS) defined as acute condition characterized by a diffused, inflammatory lung injury caused by increase pulmonary vascular permeability that induces inflammation and edema of the lungs. This process will result in changes in lung weight and loss of aerated lung tissue affecting lung compliance and the exchange of gases leading to hypoxemia [1,2].

In the case of COVID-19 pneumonia related ARDS (C-ARDS) there is also the presence of inflammation of the endothelium (endothelialitis) in the vascular system. This increases the risk for the development of thrombosis and in some cases the progression to pulmonary fibrosis [3-5].

There no too much therapeutic option for COVID-19 except for the potential benefit of the use of corticosteroids in patients with moderate and severe disease [6].

Once confirmed that there is community spread of COVID-19 in a geographical area, physicians should be highly suspicious of patients with clinical signs of respiratory symptoms (cough, wheezing, chest pain, hemoptysis), fever and progressive dyspnea.

The presence of bilateral ground glass opacities on chest CT scan, and/or conventional x rays can will help to support the diagnosis.

In severe cases (patients having C-ARDS), confusion, severe respiratory distress, cyanosis and diaphoresis can also be present [7-9]. A PCR test for SARS-CoV-2 must be performed in all patients. The test must repeated in patients who had a negative result and are showing clinical symptoms of the disease [10].

Patients with severe signs of respiratory distress will need the following criteria (using the ARDS Berlin Definition) to consider the presence of CARDS:

1. Acute onset respiratory failure that started within one week of a known clinical insult.
2. The presence of bilateral pulmonary opacities suggestive of pulmonary edema in chest x rays or CT scans, is not related to cardiac failure or fluid overload (the use of echocardiography is recommended).
3. Patients with a PaO_2/FiO_2 ratio less than 300 mm Hg receiving a minimum of a PEEP of at least 5 cm H_20 (or SpO_2/FiO_2 ratio < 315 without PEEP) [11,12].

Severity criteria

The level of hypoxemia is used to define the severity of the ARDS. The degree of impairment of oxygenation is defined by the ratio of arterial oxygen tension to the fraction of inspired oxygen ($Pa0_2/Fi0_2$).

Mild ARDS: PaO_2/FiO_2 ratio that is > 200 mmHg but < 300 mmHg that include PEEP or CPAP > 5 mmHg on the ventilator [11,12].

Moderate ARDS: PaO_2/FIO_2 ratio is > 100 mm Hg but less than < 200 mm Hg that include PEEP > 5 cm H_20 on the ventilator.

Severe ARDS: PaO_2/FIO_2 is < 100 mgHg that include PEEP > 5 cm H_20 on the ventilator.

To obtain the PaO_2/FiO_2 ratio, arterial blood gas analysis (ABGs) is required. For calculation purposes, the PaO_2 must be expressed in mmHg and the FiO_2 must be measured 0.21 and 1.00. For example, if a patient has a $Pa0_2$ of 60 mm Hg while receiving 80% of oxygen, then the PaO_2/FiO_2 ratio is 75 mmHg (60 mmHg/0.8) [10-12].

Risk factors for a non COVID-19 related ARDS

Direct insult:

- Pneumonia
- Aspiration of gastric content
- Lung contusion
- Fat embolism
- Near drowning
- Inhalation therapy
- Reperfusion injury.

Indirect insult:

- Non-pulmonary sepsis
- Multiple trauma
- Massive transfusion
- Pancreatitis
- Cardiopulmonary bypass.

Associated risk factors of severity related to COVID-19 ARDS (C-ARDS)

Elderly patients, diabetes mellitus type II (DMII), hypertension, obesity, chronic kidney disease, chronic obstructive pulmonary disease (COPD), atherosclerosis, the presence of malignancies, renal disease, immunodeficiency, and pregnancy.

Phases in the progression of lung disease related to COVID-19:

1. Early phase: (Day 0 - 1) edema, incipient epithelial damage and capillaritis/endothelialitis).

2. Exudative phase: (1 - 7 days) characterized by diffused alveolar damage (DAD), alveolar spaces contain a fibrin rich fluid, the hyaline membranes formation, type 2 pneumocyte hyperplasia and atypical regeneration sometimes with important vascular inflammation (thromboinflammation).

3. Organizing phase (one to several weeks).

4. Fibroproliferative phase: Characterized by resolution of pulmonary edema, with type II alveolar cells proliferation, myofibroblasts and interstitial infiltration, squamous metaplasia,, and early deposition of collagen. we don't know the duration of this phase, probably two to three weeks or months. Some patients progress to a fibrotic stage, characterized by obliteration of normal lung architecture, fibrosis and cyst formation. The degree of fibrosis ranges from minimal to severe [11-13].

Management and recommendations for the treatment of CARDS

Because of the unprecedented amount of patients and a rapidly evolving disease, there has been rapid changes in treatment guidelines based on scientific evidence.

To reduce the physiological impact of the disease, a proper diagnosis and treatment must be implemented. A proper initial clinical assessment, blood tests (WBC, CRP, CPT) and imaging studies (including CT scan/angio CT) must be performed. In patients with moderate to severe respiratory problems, oxygen therapy must be started. Non-invasive respiratory support (HFNC, CPAP) with close monitoring must be considered. Experience has showed that non-invasive respiratory support can reduce the need for intubation, however its prolonged use can lead to self-inflicted lung injury.

Mechanical ventilation settings

Lung protective ventilation is the recommended form of ventilatory support in patients with COVID-19, using low tidal volumes (4 - 8 ml/Kg PBW), keeping peak pressures below 30 cm H_2O, PEEP levels in between 8 - 15 cm H_2O and P below 13 cm H_2O.

In patients with refractory type of hypoxemia, the use of high levels of PEEP must be considered and tuned according to their respiratory mechanics and hemodynamic status.

The use of bedside echocardiography, lung ultrasound, $VACO_2$, lactate, $ScVO_2$ and CT Scans will help to assess for the different phenotypes and the presence of thromboembolic events [14,15]. Some adjuvants therapies are: prone positioning, inhaled nitric oxide, respiratory dialysis and ECMO as rescue therapies must be considered according to clinical progression and radiological findings [16].

Pharmacologic therapies

The use of steroids: Dexamethasone: 6 mg once daily for up to 10 days, has shown less mortality at 28 days on patients diagnosed with COVID-19 and should be recommended in all mechanically ventilated patients [17].

Therapy with low molecular weight heparins (LMWH) or with un-fractioned heparin (UFH) must be consider as a result of the high incidence of thromboembolic events in COVID -19 patients. The use of D-dimer and Factor Xa levels, cardiac and lung ultrasounds and Angio CTs can help us to optimize the screening for the risk of thrombosis [18].

The use of antimicrobials is not routinely recommended. However, bacterial co-infection at the time of the admission to the hospital and/or during the stay can occur in COVID-19 patients. Consideration for their use must be based on clinical assessment and the use of supportive diagnostic tests such as cultures, CRP, PCT and imaging studies [19,20].

Additionally, we must optimize fluid balance and using the recommended MAP levels according to international guidelines [21].

Conclusion

COVID-19 infection is a complex disease with multiorgan compromise that can have a variety of clinical presentations requiring aggressive individualized treatment from the management team, particularly when it comes to ICU patients on mechanical ventilation. Admitted patient on the ICU on mechanical ventilation still shown a high fatality rate. As the pandemic evolves, research and experience has improved our knowledge and understanding of the pathophysiology of the disease and the role of some specific drugs and ventilator strategies. However, many questions remain unanswered regarding the optimal management of these patients e.g. the role of non-invasive mechanical ventilation, when to intubate, how to choose and optimize PEEP levels, how to reduce the progression to pulmonary fibrosis and how to help on the rehabilitation and reintegration of these patients to their normal lives.

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