

Ageing Population

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Challenges in the Management of Severe SARS-CoV2 Infection in Elderly Patients

Elderly patients have damaging and serious complications when they acquire SARS-CoV2 infection. It is thus important to consider this particular age group for better management of COVID-19.

The gradual reversal of the population pyramid that has developed in recent decades has resulted in older adults being mostly affected in a pandemic situation. Senior people are the defenceless group, and the ones who have experienced the severest form of this disease. A patient who is positive for SARS-CoV2, and is over the age of 70 years old is compromised because of age. Since the beginning of this pandemic, 50% of those infected are elderly patients. The elderly also represent 33% of the total admissions in the Intensive Care Unit (ICU) and account for 22% up to 48% of the daily deceased (Bonanad 2020). This could be due to pre-existing comorbidities, geriatric syndromes, disability, dependence or frailty making them more vulnerable to this infection and poor outcomes.

Complications and Comorbidities of Ageing Adults with COVID-19

Up to 60% of senior patients with COVID-19 have at least one of the following comorbidities: hypertension, diabetes, cardiovascular disease, cerebrovascular disease, dementia, cancer, chronic kidney disease and chronic obstructive pulmonary disease (COPD). The most frequent complications of the elderly with severe COVID-19 are acute respiratory distress syndrome (ARDS), shock, delirium, acute kidney injury (AKI), myocarditis, acute

myocardial infarction, heart failure (including Takotsubo disease), arrhythmias and venous thrombosis (Li 2020; Wang 2020).

This link between elderly patients and complications should put us on an awareness mode to detect and evaluate this patient population early. Along with the clinical worsening triggered by the natural progression of the disease, medical management may also contribute to complications through the use of strategies that may not be entirely suitable for this age group. A proposed approach for the detection and diagnosis of complications of SARS-Cov2 infection for elderly patients is shown in **Table 1**.

Special Considerations in the Management of the Critically Ill Elderly Patient Due to COVID-19

Oxygen support, intubation and invasive mechanical ventilation

Oxygen therapy should be initiated when a patient presents hypoxaemia manifested by clinical signs of respiratory failure and a peripheral oxygen saturation $\leq 92\%$; in case conventional oxygen delivery devices (low-flow nasal cannulas, facial mask or oxygen reservoir bag) do not provide adequate oxygenation, another advanced type of ventilator support should be considered. Determining the appropriate time to perform intubation is a challenge in elderly patients with previous pulmonary

Complication	Diagnostic tool			Considerations
ARDS	Berlin and Kigali criteria	Timing Oxygenation PEEP requirement Chest imaging Origin of oedema	Berlin criteria Within 1 week of a known clinical insult or new or worsening respiratory symptoms. Mild: $\text{PaO}_2/\text{FiO}_2 >200$ mm Hg but <300 mm Hg. Moderate $\text{PaO}_2/\text{FiO}_2 <100$ but >200 mm Hg. Severe: $\text{PaO}_2/\text{FiO}_2 <100$ mm Hg. Minimum 5 cmH ₂ O PEEP required by invasive mechanical ventilation (non-invasive acceptable for mild ARDS) Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or CT Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic oedema if no risk factor present)	Kigali criteria Within 1 week of a known clinical insult or new or worsening respiratory symptoms $\text{SpO}_2/\text{FiO}_2 <315$ No PEEP requirement, consistent with AECC definition. Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or ultrasound Respiratory failure not fully explained by cardiac failure or fluid overload (need objective assessment, such as echocardiography, to exclude hydrostatic oedema if no risk factor present)
Shock	Shock index Diastolic shock index Clinical windows Hypotension Serum lactate Capillary refill time	Shock index: heart rate/systolic artery pressure (0.5-0.7) Diastolic shock index: heart rate/diastolic artery pressure (>2) Brain: Altered mental state Skin: Mottled, clammy Kidney: Oliguria The systolic arterial pressure is less than 90 mm Hg or the mean arterial pressure is less than 65 mm Hg. The level is increased (>1.5 mmol per litre) Capillary refill time: >2.5 s		
Myocarditis	Troponin I EKG Echocardiogram Magnetic resonance	Troponin I above the 99th percentile upper reference limit		
Acute myocardial infarction	Chest pain EKG Troponin I	Troponin I above the 99th percentile upper reference limit		
Heart failure	Symptoms. NT pro-BNP	NT-proBNP >450 pg/mL (for patients aged 75-99 years)		
Acute kidney injury	AKI KDIGO			

		AKI Stage	Serum creatinine (SCr)	Urine output
		1	1.5-1.9-fold increase in basal SCr Or increase ≥ 0.3 mg/dl	≤ 0.5 mg/kg/h for 6-12 hours
		2	Increase ≥ 2 -2.9 times in baseline SCr	≤ 0.5 ml/kg/h for > de 12 hours
		3	Initiation of renal replacement therapy (RRT), Decrease in GFR ≤ 35 ml/min/1.73 m ² in patients <18 years.	
Deep vein thrombosis	Clinical signs D-dimer Deep vein Ultrasonography	D-dimer > 0.5-1.5 mg/l		
Pulmonary embolism	D-dimer AngioCT AngioMR Echocardiogram Deep vein Ultrasonography Geneva score	Geneva score		
		Variable		Score
		Age		
		60-79 years		1
		80+ years		2
		Previous venous thromboembolism		
		Previous DVT or PE		2
		Previous surgery		
		Recent surgery within 4 weeks		3
		Heart rate		
		Heart rate >100 beats per minute		1
		PaCO₂ (partial pressure of CO₂ in arterial blood)		
		<35mmHg		2
		35-39mmHg		1
		PaO₂ (partial pressure of O₂ in arterial blood)		
		<49mmHg		4
		49-59mmHg		3
		60-71mmHg		2
		72-82mmHg		1
		Chest X-ray findings		
		Band atelectasis		1
		Elevation of hemidiaphragm		1
		The score obtained relates to the probability of the patient having had a pulmonary embolism (the lower the score, the lower the probability): <5 points indicates a low probability of PE 5-8 points indicates a moderate probability of PE >8 points indicates a high probability of PE		

Severity criteria	Lymphopenia <800 cells/ μ l C-Reactive Protein > 150 mg/l D-dimer > 0.5-1.5 mg/l Interleukin-6 >40 pg/ml Lactate dehydrogenase >350 UI/l Ferritin >1000 μ g/L Creatinine 1.5-1.9 times baseline or \geq 0.3 mg/dl increase Troponin I above the 99th percentile upper reference limit NT-proBNP >450 pg/mL (for patients aged 75-99 years)
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Table 1. Approach for early detection and diagnosis of complications of SARS-Cov2 infection in elderly patients.

pathologies like COPD or chronic cardiac failure and could excessively increase the breathing effort and generate fatigue of the inspiratory muscles rapidly compared to young adult patients. The Work of Breathing Scale (Apigo 2020) can be a useful tool. High flow nasal cannula (HFNC) or non-invasive mechanical ventilation (NVM), can be chosen alone or combined with a prone position in non-intubated patients, however, intubation should not be delayed if necessary; ROX index (Roca 2019) is useful to make the decision in these cases. Protective mechanical ventilation is a cornerstone in the treatment of ARDS. It is recommended to start with a tidal volume of 6 ml/kg of predicted weight and maintain a plateau pressure <30 cm H₂O. An acceptable goal of oxygenation in patients with ARDS is 88 to 94% arterial peripheral oxygen saturation (SaO₂). However, in patients with ischaemic heart disease, it may be more advisable to maintain oxygenation values above 90%.

Analgesia and sedation

In patients with invasive mechanical ventilation (IMV), a target of sedation and analgesia should be established using the RASS scale CPOF scale. Propofol and dexmedetomidine are recommended over the use of benzodiazepines. The use of opioids such as fentanyl as adjuvant treatment with paracetamol is recommended in order to reduce the total dose of morphine derivatives. Long-term use of benzodiazepines and opioids can trigger delirium.

It is recommended to remove sedatives as soon as possible and implement daily sedation withdrawal strategies in patients who present clinical improvement. The use of tramadol and antineuritic medications such as gabapentin may be considered. We suggest avoiding routine use of NSAIDs due to the high risk of complications such as AKI and gastrointestinal bleeding.

Specific therapies

Dexamethasone is recommended for COVID-19 patients who are hypoxaemic or under IMV. Special care must be taken with increases in blood glucose and weakness in the critically ill patients. Lopinavir-ritonavir, hydroxychloroquine with or without azithromycin are not recommended (RECOVERY 2020) due to greater predisposition to QT prolongation and arrhythmias in this group of patients. Tocilizumab is not recommended either (CONVACTA 2020). Remdesivir and other antiviral drugs are still being tested in clinical trials.

Prophylaxis for venous thrombosis and anticoagulation

It is recommended to use low molecular weight heparin, such as enoxaparin for thromboprophylaxis in all hospitalised patients and to facilitate early mobilisation to avoid venous thrombosis, especially because older adults present comorbidities that generate a higher prothrombotic risk such as immobility, disabling cerebrovascular disease, hip or pelvic limb fracture,

malignancy, etc. In case of clinical data of deep vein thrombosis, it is recommended to perform Doppler ultrasound for diagnosis. If venous thrombotic episode is confirmed, the anticoagulant dose should be increased. The dose should be adjusted based on renal function. Patients receiving oral anticoagulants should be switched to enoxaparin during their hospitalisation and their usual treatment should be restored upon admission.

Fluid therapy

Intravenous fluid therapy has traditionally been considered a standard of treatment in patients with sepsis. However, large volumes of intravenous fluids (as initially recommended by the Guidelines of Surviving Sepsis Campaign) in elderly patients, can lead to fluid overload, increase hypoxaemia, contribute to AKI and other adverse effects. Therefore, fluid restrictive therapy is recommended in patients with ARDS from COVID-19. In case of hypotension and shock, dynamic fluid response manoeuvres are suggested to make the decision to indicate crystalloid infusion, over static manoeuvres, or liberal fluid therapy. Hydroxyethyl starches are not recommended due to the risk of AKI.

Vasopressors, inotropes and adjuvants

In the management of elderly patients in shock, it is recommended to start norepinephrine early to rapidly improve organ perfusion and avoid unnecessary infusions of intravenous crystalloids with

a target of mean arterial pressure (MAP) close to 65 mm Hg, monitoring capillary refilling and other perfusion data obtained by the clinic. Pursuing a target of MAP close to 80 mm Hg can lead to atrial fibrillation in elderly patients and is therefore, not recommended. The use of hydrocortisone and a second vasopressor with a different mechanism of action as vasopressin is also justified given the suspicion of refractory vasodilation. The use of inotropic drugs like dobutamine should be considered when considering cardiogenic shock due to complications such as acute myocardial infarction or septic cardiomyopathy, which are relatively frequent in this group of patients. An echocardiogram is useful for making decisions. Esmolol or ivabradine could be used as adjuvant therapy for refractory shock in the event of suspected diastolic dysfunction due to sepsis, since elderly patients may initially present difficulty in myocardial relaxation due to their age or due to hypertensive heart disease.

Renal replacement therapy

Chronic kidney disease (CKD) is most associated with mortality in patients with COVID-19. When faced with a patient who previously required renal replacement therapy (RRT) (dialysis or haemodialysis) or generates AKI refractory to medical treatment, a renal replacement strategy should be considered. An appropriate option for haemodynamically unstable patients is the use of continuous or intermittent slow therapies. However, adverse events such as thrombocytopenia, hypocalcaemia (in

case of use of citrate) or rapid intravascular volume removal should be anticipated to avoid complications. The use of sodium bicarbonate could decrease the need for RRT in selected cases (Jaber 2018).

Prevention and treatment of delirium

It is important to use an adapted room without conditions that predispose to delirium: adequate lighting during the day and darkness at night, a visible clock, television, ambient sounds or music, communication tools for visual and digital communication with health personnel, mobile phone to have contact with family and physical therapy and occupational therapy. Avoid unnecessary invasive devices and remove those already used as soon as possible, including catheters, urinary catheters and restrictions. Special caution should be exercised in the prescription of drugs associated with delirium (H2 antagonists, prokinetics such as metoclopramide, some antibiotics, sedatives, analgesics, etc.) Drugs such as olanzapine, quetiapine or risperidone are indicated as specific treatment but lack clinical evidence. Special caution should be exercised with the use of haloperidol in this group of patients. It is recommended to start at low doses with close monitoring of cardiac rhythm.

Palliative care

Being aware of the high lethality of elderly patients with COVID-19, patients with poor prognosis, multiorgan failure, severity scales such as the acute physiology and chronic health disease classification system

II (APACHEII) and sequential organic failure assessment (SOFA) elevated and that do not respond adequately to treatment, the possibility of limiting the therapeutic effort should be considered in order to avoid cruelty. Communication with family members should be established to make the decision properly.

Conclusion

Elderly patients with severe SARS-CoV2 virus infection have higher mortality than other age groups. This is primarily due to their comorbidities. The individualisation of management in this patient population plays an important role and should always be done based on the best available evidence adapted to the clinical setting.

Conflict of Interest

The authors declare no conflicts of interest. ■

Key Points

- Senior people are the defenceless group and the ones who have experienced the severest form of COVID-19 disease.
- Senior patients with COVID-19 have at least one of the following comorbidities: hypertension, diabetes, cardiovascular disease, cerebrovascular disease, dementia, cancer, chronic kidney disease and chronic obstructive pulmonary disease (COPD).
- Frequent complications of the elderly with severe COVID-19 are acute respiratory distress syndrome (ARDS), shock, delirium, acute kidney injury (AKI), myocarditis, acute myocardial infarction, heart failure, arrhythmias and venous thrombosis.
- The individualisation of management in this patient population plays an important role and should always be done based on the best available evidence adapted to the clinical setting.

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