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RESPIRATORY MANAGEMENT PROTOCOL OF PATIENTS WITH SARS-COV-2 (COVID-19)

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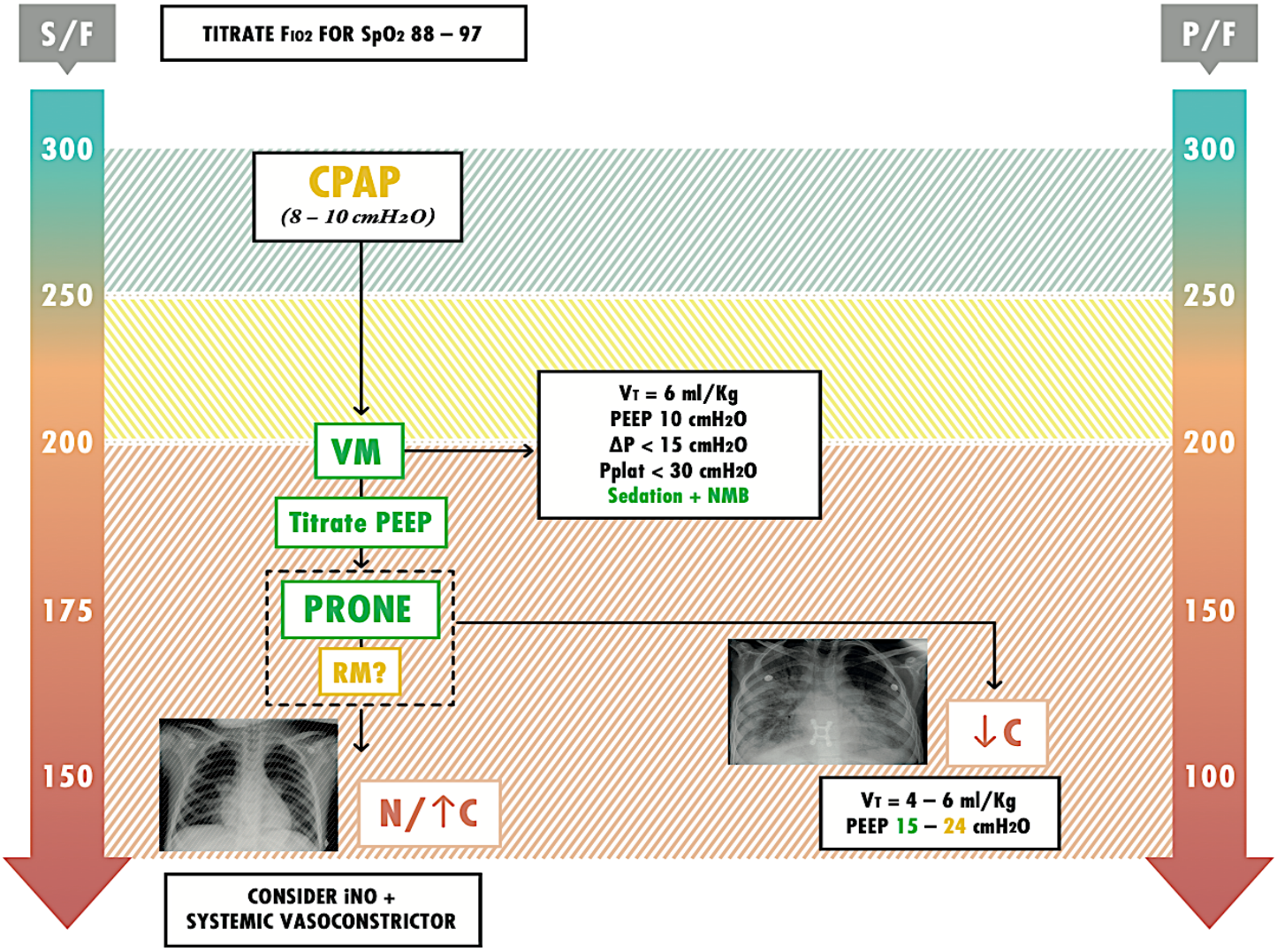

EVIDENCE LEVEL

Highly recommended

Little recommended

Not recommended

INTRODUCTION

Based on what has been currently published by the Chinese, Italians, UK, USA and the Spanish, we believe it is necessary to develop a unified action criteria in order to optimise resources and apply the most effective therapies for patients with COVID-19. While there have been consensus guidelines for ventilator management with COVID-19, including those created by the Surviving Sepsis Collaborative and the American Association of Respiratory Care (AARC), many recommendations are based on evidence generated from patients with more classic ARDS. From the published literature to date, coupled with direct patient observation, we believe modifications to these recommendations should be considered.

It appears that in many patients, the type of hypoxemic respiratory failure resulting from COVID-19 may differ from more classic forms of Acute Respiratory Distress Syndrome (ARDS)(1). While many patients have significant loss of end expiratory lung volume, compliance is often relatively preserved with high degrees of alveolar dead-space, suggesting possible alteration of the hypoxic pulmonary vasoconstriction (HPV) reflex (2), or other mechanisms yet to be found.

In relation to the above we recommend that in patients with respiratory failure related to COVID-19:

1. The degree of oxygen impairment should be measured routinely using **pulse oximetry/inspired fraction of oxygen ratio (S/F)** (3)(4)(5). S/F is recommended to assess patient evolution and is non-invasive, available to all patients. Taking into account the large number of patients to be treated, the S/F will be very useful as it is non-invasive. The **PaO_2/FiO_2 ratio (P/F)** is the **gold standard**(3) (6) to measure oxygen impairment but it can be reserved for patients with more severe disease, haemodynamic instability (needing invasive blood pressure monitoring), or for confirmation of S/F. It is important to instruct medical staff in the proper measurement of the S/F, which includes titration of FiO2 to achieve a saturation between 88 - 97%. *[Figure 1]*
    - In paediatric patients Oxygen Index (OI) and Oxygen Saturation Index (OSI) can be used to guide the treatment approach. (7)

2. High flow oxygen therapy (HFNC). High flow oxygen therapy (HFNC) can be considered for patients who do not have severe hypoxemia, particularly if the availability of ventilators is limited. However HFNC may have increased risks for aerosolization of the virus. The response to HFNC must be assessed within 30 – 60 minutes of initiation, and patients who do not improve significantly should not be maintained on HFNC. It is important to remember that HFNC does not produce significant lung recruitment.(8)(9)(10) If a patient on HFNC has sustained moderate/severe hypoxemia (S/F < 220; FiO_2 > 0.4 for SpO_2 > 92%) escalation to another form of respiratory support (NIV or intubation) should be strongly considered, depending on availability of resources.

    If HFNC is being used, there is risk of aerosol generation which poses an infection risk to the medical staff. In this sense, the use of HFNC in a negative pressure room with airborne precautions is highly recommended, if available.

    - Oxygen therapy with mask with a reservoir. While this can deliver high amounts of oxygen, we believe this type of device should not be used since it does not generate recruitment of the lungs. Furthermore, administering 100% oxygen will cause an increase in PaO_2 and SpO_2 with no improvement in P/F ratio (shunt, recruitment), which may lead to a delay in the administration of an adequate recruitment therapy, such as positive pressure ventilation (CPAP/BLPAP, IMV).

3. **EARLY CPAP/BLPAP.** Should be considered if the patient has significant oxygen need or high work of breathing. The response to CPAP/BLPAP must be assessed within 30 minutes of initiation, and those who do not improve significantly should be intubated. If the patient on NIV has sustained moderate/severe hypoxemia (S/F < 200; FiO_2 > 0.4), intubation

should be strongly considered, depending on availability of resources. The helmet(11) is recommended as the first line interface to be used, if available. When CPAP is provided using home care ventilators, it is important to remember the limitation in the administration of FiO_2 (i.e. due to T piece). This reinforces the importance of close patient monitoring (S/F).

It is important to consider that double limb circuits are recommended. However, single limb circuits can be used. In this case, it is important to insert a filter in between the patient and the expiratory port or directly on the expiratory port, depending on the different interfaces (vented interfaces and interfaces with anti-asphyxia valves are not recommended) available.

As a summary, the use of non-invasive support has to be adapted to the local circumstances (equipment, personal, etc.).

- Like HFNC, there is a risk for aerosolization of the virus with CPAP/BLPAP. This risk may be lower with the helmet interface. In the event that a helmet is not available, a total face mask interface would be the next choice. We advise the use of airborne precautions and negative pressure rooms if possible whenever CPAP/BLPAP is being used.

4. **INTUBATION.** If resources are available, the patient should be intubated if they maintain a P/F or S/F ≤ 200 (FiO_2 > 0.4) after initiation of non-invasive therapy. If the patient is treated with NIV or HFNC and presents with high work of breathing (WOB) even if P/F or S/F is > 200 (FiO_2 < 0.4 for SpO_2 > 92%), they should be intubated. A surrogate marker which can be used for guidance about work of breathing is the *ROX index [(S/F) / RR]* (12). If the patient has a ROX index ≤ 5 intubation is strongly advised. Chest X-Ray or lung ultrasound or chest CT should be performed to assess for ground glass opacities and the distribution of pulmonary opacifications. Static lung compliance (C) (13) should also be evaluated after intubation, with no spontaneous breathing present (flow zero).

5. **INITIAL SETTINGS.** Protective Ventilation. Since many of these patients have normal or high Respiratory System Compliance (C), it is recommended (14):

    a. Standard sedation (controlled by SAS / RASS) + Neuromuscular Blockade. Continuous neuromuscular blockade should be considered for the first 24 – 48 hours after intubation (15), although intermittent neuromuscular blockade is also reasonable given limited availability of neuromuscular blocking medications in some countries.

b. Initial PEEP: 10 cmH_2O. (16) (17)
c. VT: 6 ml/kg of IBW. (18) (19)
d. Driving Pressure: < 15 cmH_2O. (20) (21)
e. Pplat: < 30 cmH_2O. (22)(23)
f. FiO_2 to achieve oxygen saturation between 88-97%

6. **NO IMPROVEMENT.** If P/F ratio remains < 200, consider the following:

A. If P/F between 151 – 200 or S/F 176 – 200 (FiO_2 0.4 – 0.5), perform a PEEP express titration (24)(25)(26)(27) *[Figure 2]*:

a. Initial PEEP: 10 cmH_2O. (28)
b. Increase PEEP 2 cmH_2O, every 2 minutes. Measure plateau pressure, and monitor oxygenation response (S/F ratio).
c. Set the highest PEEP that maintains or improves S/F ratio and allows a Pplat of ≤ 30 cmH_2O.

B. If P/F ≤ 150 or S/F ≤ 175 (FiO_2 > 0.5) after the express PEEP titration. The following therapeutic options would be recommended:

a. ***PRONE POSITIONING.*** (29) (30) (31) (32) This should be considered as the first line of treatment if resources in the ICU are available. The evidence suggests it is most useful for patients with P/F ≤ 150, and is not recommended if P/F is above. Recommended approach (2 options):

- Place Prone and evaluate response: If improvement in P/F – S/F ratio when placing prone, maintain in prone position for at least 16 hours and until P/F or S/F ratio >200 for at least 4 hours. Turn supine. If patient is able to maintain P/F >150 or S/F > 175 for at least 4 hours remain supine. Otherwise prone again for at least 16 hours and re-evaluate.
- If resources are available, rotation between prone and supine positioning should be considered following the recommendations above, with duration of prone ranging from 16-20 hours a day.
- It is important to considerer that most patients can suffer a decrease of P/F ratio after changing from prone to supine position.

b. ***RECRUITMENT MANEUVRES.*** (33) (34) (35) (36) This could be considered prior to prone positioning if resources are limited. They may also be considered for patients that are Prone but persist with P/F < 150 or S/F < 175. Careful consideration of haemodynamics must be considered before and during the recruitment maneuvers. Recruitment maneuvres should be performed under careful monitoring.

- We suggest increasing the PEEP initially to 10, then 15 and finally up to 20 cmH_2O with 0-30 seconds at each step, in PCV mode. Limit the delta pressure (Peak Inspiratory Pressure-PEEP) to no more than 15 cmH_20 during this maneuver. Then switch to volume control ventilation and titrate the PEEP decrementally by the lowest Driving Pressure. One option would be to follow the modified Amato algorithm *[Figure 3]*.

- Different methods of recruitment can be attempted as per usual local practice, but no single method can be recommended based on current evidence. Safety of the patient has to be ensured during any RM(33). RM should be used with extreme caution in patients with cardiac disease or hemodynamic instability.

- Cardiac ultrasound in addition to lung ultrasound is highly recommended when PEEP level is being titrated or during recruitment maneuvres. Patients with more preserved lung compliance will be more likely to suffer an increase in pulmonary arterial pressure (PAP) or impairment in venous return as PEEP is escalated, particularly if the consolidated areas of lung are not able to be recruited.

7. **If hypoxemia is refractory** (P/F < 150 or S/F < 175) despite prone and RM, two options should be considered:

    1. *ARDS with a predominance of alteration of the HPV reflex.* (37) (38) This possibility should be considered in a patient with few alveolar-interstitial infiltrates (¨Black X-ray¨) and poor response to recruitment techniques (PEEP increments, proning and recruitment maneuvres). In this case, the use of iNO + systemic vasoconstrictors (39) (40) should be considered, particularly if there are signs of the pulmonary hypertension on echography.

The chest X-ray does not often reveal the extent of the problem. In many cases the X-ray is relatively normal, but the CT is very altered. Lung ultrasound is recommended for the diagnosis and to guide the treatment approach.(41)
The use of ECMO as an initial treatment strategy is not recommended; but this should be left to the evaluation by medical staff on a case by case basis.

2. *Classic ARDS.* Chest X-ray with a clear bilateral alveolar-interstitial infiltrate pattern and low C. (42)(43) A higher PEEP and lower tidal volume strategy should be considered:

- PEEP = 12 - 24 cmH_2O. (44)
- VT = 4 – 6 ml/kg IBW.
- Driving Pressure: < 15 cmH_2O.
- Pplat: < 30 cmH_2O.

- In these circumstances, the express PEEP titration or the Recruitment Manuevers followed by PEEP titration described above should be followed.

- Some patients with a typical ARDS may need levels above 15 – 18 cmH_2O of PEEP. It is important to ensure that the patient is responding favourably as PEEP is escalated. The following criteria should be considered to gauge if higher PEEP levels are helping the patient:

    1. Improvement in oxygenation as measured by an increase in P/F ratio by at least 25 points. If this improvement in the P/F ratio is not observed after the increase in the PEEP level, it would be advisable to maintain the previous level of PEEP.(45)
    2. Improvement in static compliance, as measured by a reduction in driving pressure if volume control ventilation is used, or improvement in tidal volume for the same delta pressure if pressure control ventilation is used.
    3. No significant worsening of hemodynamics.

S/F concept
(Figure 1)

Titrate FiO_2 for SpO_2 = 95% ⇒ PaO_2 = 80 mmHg

FiO_2	S/F	P/F	SHUNT	RISK
0.3	300	270	20%	
0.4	250	200	30%	
0.5	200	160	40%	
0,6	160	130	50%	
0.7	135	120		
0.8	120	100	> 50%	
0.9	100	90		
1	< 100	80		

High PEEP Recommended Strategy
Express
(Figure 2)

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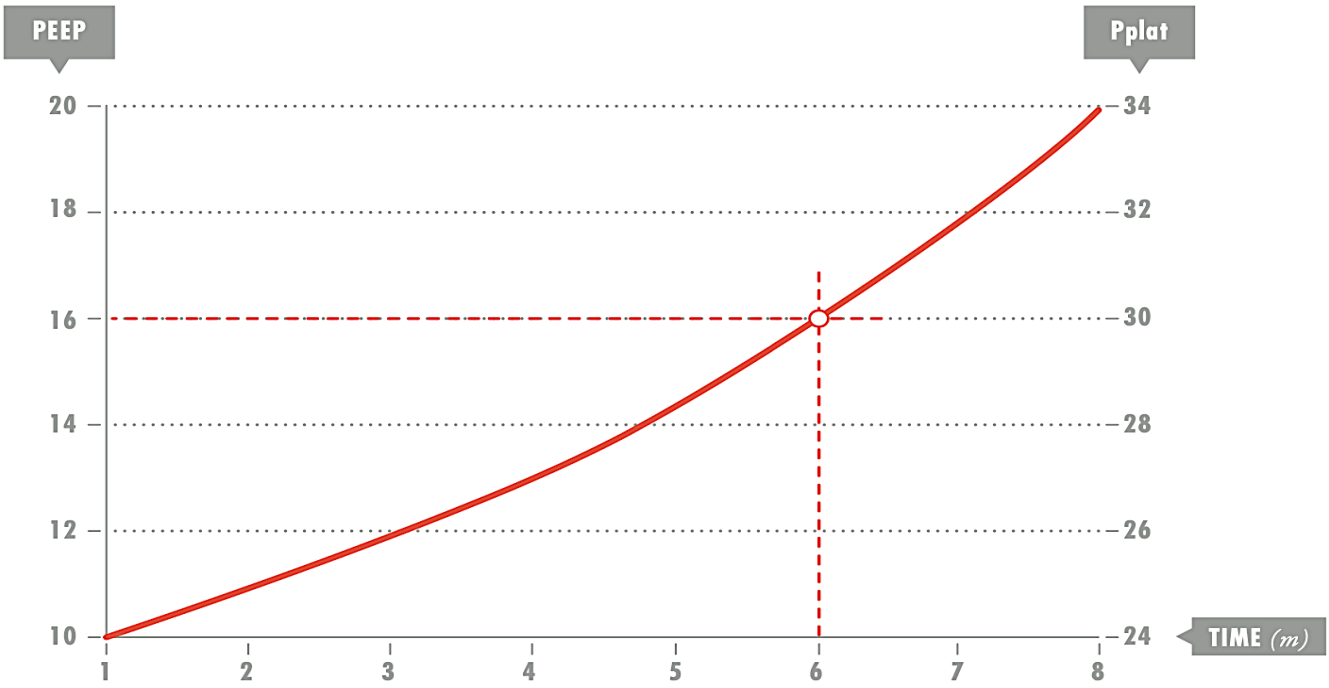
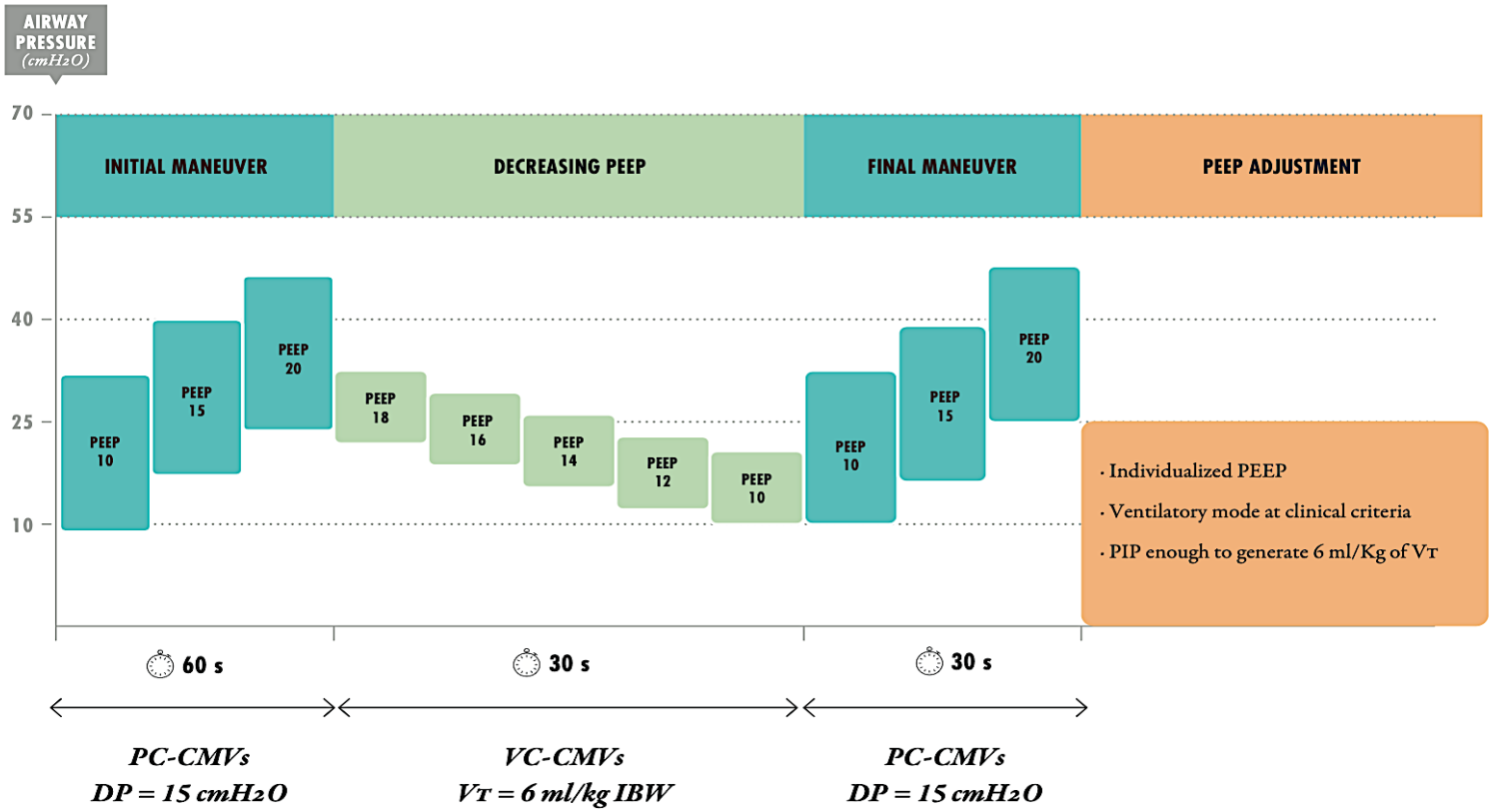


Decreasing titration of PEEP
Protocol Prof. Amato (modified)

(Figure 3)



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