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Optimizing respiratory care in coronavirus disease-2019: A comprehensive, protocolized, evidence-based, algorithmic approach

Sagar Sinha, Indrani Sardesai[1], Sagar C. Galwankar[2], P.W.B. Nanayakkara[3], Dindigal Ramakrishnan Narasimhan, Joydeep Grover[4], Harry L. Anderson III[5], Lorenzo Paladino[6], David F. Gaieski[7], Salvatore Di Somma[8], Stanislaw P. Stawicki[9]

Key Words: Coronavirus disease 2019, respiratory care optimization, clinical algorithm, SARS-CoV-2, evidence-based guideline, resource-sparing strategies

INTRODUCTION

Respiratory management of patients with corona virus disease 2019 (COVID-19) is both complex and highly nuanced.[1] Although most patients with COVID-19 develop mild or no symptoms, a smaller proportion (up to 15%) experience progressive hypoxic respiratory failure requiring escalating levels of oxygen support.[2] Significant accumulated experience in caring for patients with SARS-CoV-2 pulmonary illness resulted in the recognition of major respiratory failure patterns, the benefits of early proning, and the importance of a step-wise escalation in levels of invasiveness across the entire spectrum from nasal cannula to extracorporeal support.[2-4] Given substantial heterogeneity among various algorithmic approaches to oxygen therapy and the need for both standardization and optimization of clinical management methodologies, the Joint ACAIM-WACEM COVID-19 Clinical Management Taskforce (CCMT) set out to establish and publish a unified approach to the patient who presents with SARS-CoV-2 lower respiratory tract infection (LRTI). In addition, the CCMT hopes that a protocol-driven strategy will lead to conservation of precious healthcare resources, such as intensive care beds and ventilators, by eliminating unnecessary interventions and various other process inefficiencies.

Clinical rationale

The Joint ACAIM-WACEM CCMT is a multidisciplinary group with participants from multiple countries and significant collective expertise in clinical management of COVID-19. Based on our shared experiences, we set

Department of Critical Care and Emergency Medicine, MGM Medical College and Hospital, Navi Mumbai, Maharashtra, India, [1]Department of Accident and Emergency Medicine, Queen Elizabeth Hospital, Gateshead, [4]Department of Emergency Medicine, Southmead Hospital, Bristol, England, United Kingdom, [2]Department of Emergency Medicine, Sarasota Memorial Hospital, Florida State University, Sarasota, Florida, [5]Department of Surgery, St. Joseph Mercy Ann Arbor, Ann Arbor, Michigan, [6]Department of Emergency Medicine, SUNY Downstate and Kings County Hospital Medical Center, New York, [7]Department of Emergency Medicine, Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, [9]Department of Research and Innovation, St. Luke's University Health Network, Bethlehem, Pennsylvania, USA, [3]Section General and Acute Internal Medicine, Amsterdam UMC, Location VU University Medical Center, Amsterdam, the Netherlands, [8]Department of Medical-Surgical Sciences and Translational Medicine, University of Rome "Sapienza," Rome, Italy

Address for correspondence:
Dr. Indrani Sardesai,
C/O Accident and Emergency Medicine Office, Queen Elizabeth Hospital, Queen Elizabeth Avenue, Gateshead, Tyne and Wear NE96SX, United Kingdom.
E-mail: isardesai@gmail.com

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out to design and optimize a uniform approach toward patients suffering from SARS-CoV-2 LRTI. The primary goal of the CCMT was to ensure broad applicability of the resultant treatment algorithms across diverse clinical settings, regardless of resource availability [Table 1]. The secondary goal was to produce a comprehensive, evidence-based resource that will provide clinicians with an easy-to-use and powerful set of tools to manage COVID-19 patients with LRTI and respiratory failure. Multiple sources were utilized when compiling this collection of algorithms and tables.[2,5-20]

The working hypothesis adopted by the CCMT is that in COVID-19, the disease caused by SARS-CoV-2 manifests primarily as an oxygen diffusion problem rather than as alterations involving ventilation-perfusion (V/Q) mismatch, low fraction of inspired oxygen (FiO_2), or hypoventilation.[1,3,4,11] Consequently, we advocate that initial attempts to address the oxygenation-related impairment should include low-flow nasal cannula (LFNC) and reservoir masks, with progressive escalation to high-flow nasal cannula (HFNC) before implementing awake proning or non-invasive positive pressure ventilation (NIPPV).[11,14,15,21,22] If these maneuvers and strategies are ineffective, we advocate that a prompt transition is made toward invasive mechanical ventilatory support.[14,22,23] Cumulatively, the above approach serves to optimize and standardize the overall management of COVID-19 patients with LRTI. The rationale for applying different oxygen therapies to different primary pathophysiologic respiratory problems is presented in Table 2.

Table 1: Comparison between resource-abundant and resource-limited health-care settings

Setting/environment/safety	Resource abundant + patient centered	Resource limited + HCP centered
Phase of pandemic	1, 2	3, 4
Infrastructure	Adequate	Average
Hospital occupancy	Low	High
Surge ICU beds	No	Yes
Regular health-care providers	Yes	No
Dedicated CCM services	Yes	No

The joint ACAIM-WACEM COVID-19 Clinical management Taskforce recognizes that there exist significant regional variations in terms of health-care resources, including considerations related to infrastructure, capacity, clinical skillset, equipment, access/availability, and other resources essential for patient care. ICU: Intensive care unit, HCP: Health-care provider, CCM: Critical care medicine, COVID-19: Coronavirus disease 2019

Patient history and clinical assessment

Infection with COVID-19 should be suspected in patients presenting with "typical" signs and symptoms including fever, cough, and various degrees of hypoxia,[24] although clinical manifestations can take a number of other forms, particularly in the elderly population.[2] Patients with elevated risk of severe disease are older, immunocompromised, morbidly obese, male, or have two or more chronic comorbid conditions.[2,24-26] Additional clinical signs and symptoms associated with severe illness include tachycardia, hyperthermia (≥39°C), encephalopathy, and hemodynamic instability.[2,27] While a "typical" COVID-19 presentation is seen in the vast majority of cases,[2] additional specific "red flags" such as the presence of "silent hypoxia" must be kept in mind.[27-30] Reliable oxygen saturation measurement (SpO_2) is the cornerstone of initial risk stratification and disease severity assessment. Patients with normal (or "baseline," if preexisting pulmonary disease exists) SpO_2 are stratified as "low risk," whereas patients with an initial SpO_2 < 93% (or similar decline below "baseline" levels) require immediate supplemental oxygen therapy.

In addition to a comprehensive COVID-19 laboratory workup,[2,31] specific factors associated with severe respiratory disease have been identified, including the presence of myalgias, elevated hemoglobin levels, and elevated alanine aminotransferase.[2] Specific risk assessment tools may be considered including the MuLBSTA[32] and BCRSS scores.[2,33] Moreover, laboratory findings of a neutrophil-to-lymphocyte ratio of >3.3,

Table 2: Oxygen therapies and respiratory pathophysiology, including evidence-based support

	Oxygenation	Ventilation	WOB	Solves diffusion	Solves V/Q mismatch	Solves recruitment
LFNC	+	-	-	+	-	-
Reservoir mask	+ +	-	+/-	+ +	-	+
HFNC	+ + +	+/-	+/-	+ + +	-	-
Awake proning	+	+	-	-	+ +	+
HFNC + awake proning	+ + +	+ +	-	+ +/(H)	+ +/(H)	+/(H)
CPAP (no O_2)	-	+/-	+/-	-	+	+
CPAP (with O_2)	+	+/-	+/-	+	+	+
NIPPV (no O_2)	-	+ +	+ +	+/-	+	+
NIPPV (with O_2)	+	+ +	+ +	+	+	+
IMV	+ +	+ +	+ +	+ +	+ +	+ +
IMV + proning	+ +	+ +	+ +	+ +	+ + +	+ + +
ECLS	+ + +	+ + +	+ + +	NA	NA	NA

H: Based on past evidence, but largely hypothetical in the context of COVID-19 lower respiratory disease. WOB: Work of breathing, LFNC: Low-flow nasal cannula, HFNC: High-flow nasal cannula, V/Q mismatch: Ventilation-perfusion mismatch, CPAP: Continuous positive airway pressure, NIPPV: Noninvasive positive pressure ventilation, IMV: Invasive mechanical ventilation, ECLS: Extracorporeal life support, COVID-19: Coronavirus disease 2019, + / + + / + + + Denotes the level of available evidence, with "+/-" and "-" denoting insufficient or lack of supporting evidence, respectively

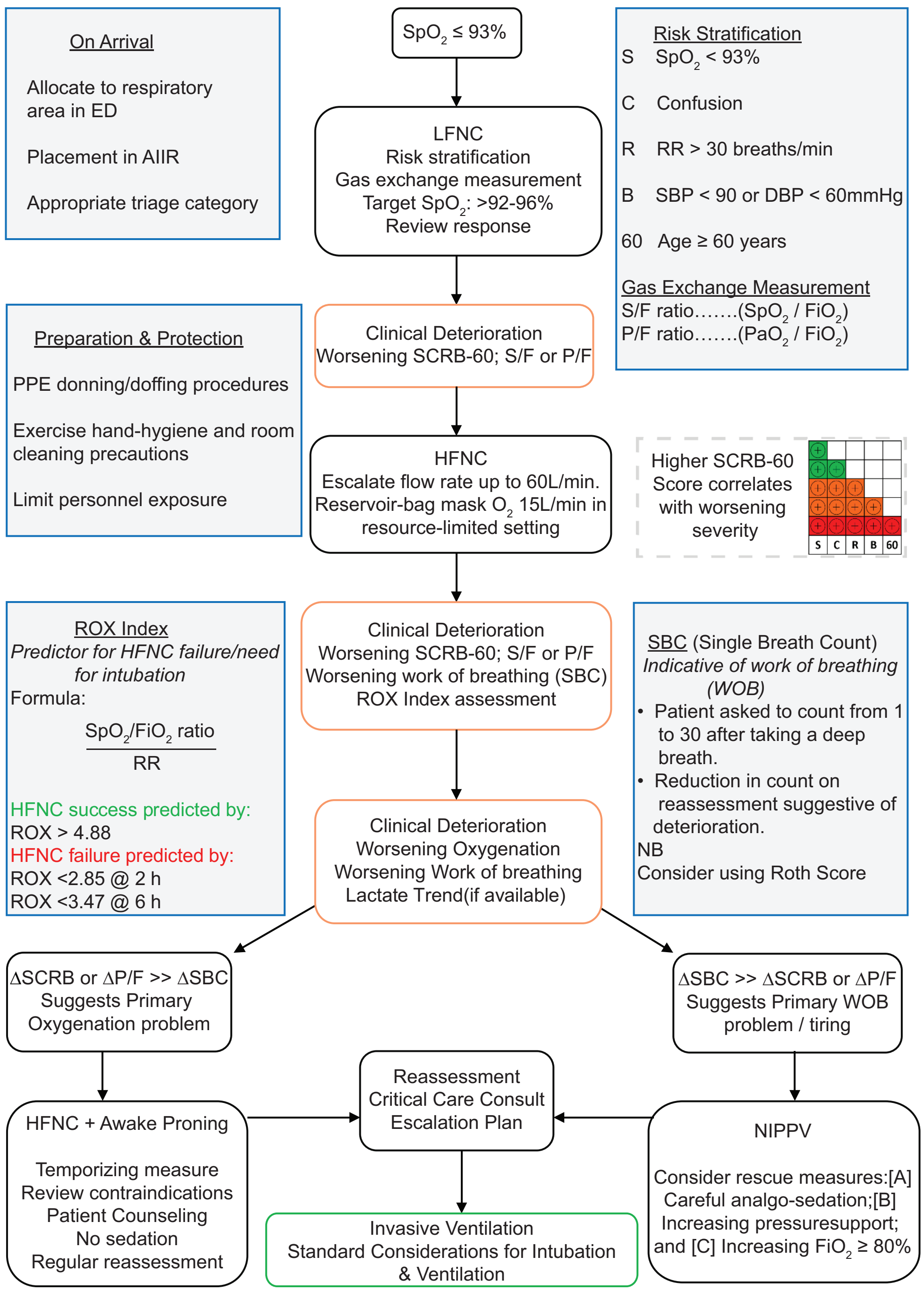

Figure 1: Management algorithm for nonintubated coronavirus disease-2019 patients with progressive respiratory worsening. AIIR: Airborne infection isolation room, LFNC: Low-flow nasal cannula, HFNC: High-flow nasal cannula, S/F: SpO_2/FiO_2, P/F: PaO_2/FiO_2, PPE: Personal protective equipment, SpO_2: Peripheral capillary oxygen saturation, RR: Respiratory rate, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, SBC: Single breath count, Δ: change, NIPPV: Noninvasive positive pressure ventilation, WOB: Work of breathing

thrombocytopenia, markedly elevated D-dimer, and early elevations in highly sensitive troponin, are all linked to severe disease and poorer prognosis.[2,34-37] Severe COVID-19 may also be associated with elevated risk of thromboembolic events.[38]

Pertinent diagnostic and clinical monitoring criteria

Radiographic workup is an important part of the overall COVID-19 patient assessment. The initial chest radiograph shows "typical" diagnostic changes in >67% of patients, and this may increase to >95% in cases of severe disease.[35] Noncontrast computed tomography (NCCT) of the chest may correlate with both the diagnosis and severity of COVID 19, and has a reported sensitivity of >90% at 2–5 days post-onset of symptoms and 97% sensitivity thereafter.[2,39,40] If the NCCT findings are suspicious for COVID-19,[41] low-molecular-weight heparin administration[42] and hospital admission should be considered. If the NCCT is not suggestive of COVID-19, then contrast-enhanced

Table 3: Patient monitoring criteria grouped by both patient location and resource-based considerations

Location	Resource abundant	Resource limited
TRIAGE	On arrival SpO_2	On arrival SpO_2
Emergency department (or high-dependency units)	On arrival + every 2 h Prognosticators PaO_2/FiO_2: Ideal SpO_2/FiO_2: Quick or used in combination Clinical risk stratification SCRB-60 SCRUB-60 ED/wards	On arrival + every 4-6 h Prognosticators SpO_2/FiO_2: Acceptable Clinical risk stratification SCRB-60 SCRUB-60 wards
High-dependency units or intensive care units	Prognosticators PaO_2/FiO_2: Ideal Clinical risk stratification SCRUB-60 SPS-II/APACHE-II	Prognosticators PaO_2/FiO_2: Ideal SpO_2/FiO_2: Used in combination Clinical risk stratification SCRUB-60 SAPS-II/APACHE-II

APACHE-II: Acute Physiology and Chronic Health Evaluation II, ED: Emergency department, FiO_2: Fraction of inspired oxygen, SCRB-60: Proposed severity score [Table 4], SAPS-II: Simplified Acute Physiology Score II, SpO_2: Peripheral capillary oxygen saturation

Table 4: The SCR(U)B-60 tool used for risk stratification of community-acquired pneumonia

S: SpO_2 <93%
C: Confusion
R: Respiratory rate >30 breaths/min
U: Urea >7 mmol/L (>19 mg/dL)
B: Blood pressure <90 mmHg (systolic) or <60 mmHg (diastolic)
60: Age 60 years, modified to account for higher mortality in COVID for age ≥60 years

The tool is a modification of the CURB-65 score.[43-45] The basic SCRB score can be supplemented with urea (U) measurement when it becomes available. COVID-19: Coronavirus disease 2019

Table 5: The single breath count tool[47,48]

Method
Step 1: Ask patient to take a deep breath
Step 2: Patient counts from 1 to 30 in a single breath
Step 3: Record time taken to count 1 to highest number, in seconds
Step 4: Ask patient to take three further deep breaths
Step 5: Repeat from steps 1 to 3

One may also consider the Breathlessness Screening Tool (BST) where the patient counts from 1 to 30 in their native language. Times between consecutive breaths <8 s correlate with the risk of SpO_2 <95% with sensitivity/specificity of 78%/71%, while times <5 s increase sensitivity to 91%[48]

CT of the chest or V/Q scanning may be considered to rule out other causes of hypoxia.

Specific clinical monitoring criteria, as directly relevant to the current manuscript, can be stratified according to patient/assessment location as well as the overall resource availability [Table 3]. Within this larger paradigm, several assessment tools need to be introduced, including the SCRUB-60 tool [Table 4][43-45] and the SBC tool [Table 5].[46-48] Finally, the risk of pneumothorax may be elevated in patients on prolonged positive pressure ventilation, necessitating tube thoracostomy placement when indicated.[49]

Determination of response to therapy and therapeutic escalation points

As one moves along the respiratory management algorithm, the need arises for standardized clinical checkpoints performed with a regular frequency [Table 6]. Finally, predetermined therapeutic escalation points will be important to ensure standardized application of the algorithm across different disease acuity levels [Table 7].[20]

Mechanical ventilation, proning, and extracorporeal mechanical support

Given that at least two distinct phenotypes of respiratory failure exist in COVID-19, prompt recognition of the type (L vs. H) of physiology applicable to each particular patient, followed by appropriate mechanical ventilation strategy, will be critical [Table 8].[51,52] In addition, early and aggressive proning strategy, beginning while the patient is still on nasal cannula oxygen therapy (i.e., a strategy aimed at preventing tracheal intubation) and continuing along the entire spectrum of respiratory failure severity, is now considered critical to achieving favorable clinical outcomes.[2,53] Finally, important considerations and limitations to prone positioning therapy are provided in Table 9. In terms of extracorporeal mechanical support, providers should follow established guidelines and appropriate patient suitability criteria to optimize clinical outcomes.[2]

SUMMARY AND CONCLUSIONS

Summative algorithms for initial management of nonintubated COVID-19 patients [Figure 1]; basic mechanical ventilation approaches [Figure 2]; and advanced mechanical ventilation strategies for more severely ill patients [Figure 3] are presented at this time.[56-58] In addition, one should be ready to recognize when appropriate escalation of care transitions may be required, keeping in mind that there must be a balance between indiscriminately following a "protocol" and patient-centric consideration for individual circumstances. With that in mind, standardizing documentation ensures that all teams involved in caring for the patient remain updated and aware of previous discussions, decisions, and potential changes [Figure 4]. It is important to recognize that our understanding of SARS-CoV-2 and COVID-19 continues to evolve, and that current management strategies may change in response to increased medical and scientific knowledge of the disease process.

Special note

A full discussion regarding the complex issue of monitoring and maintaining adequate oxygenation in the outpatient/home setting is beyond the scope of this

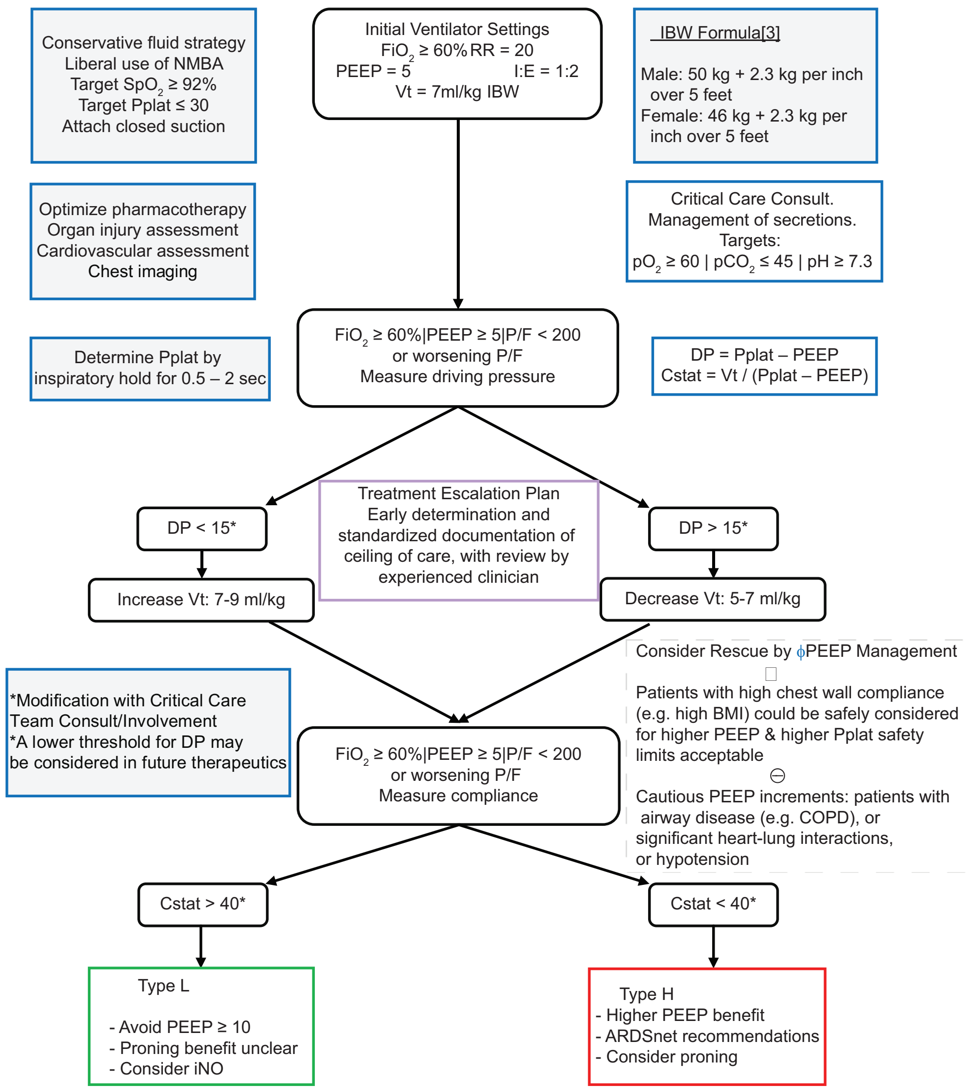

Figure 2: Management algorithm for coronavirus disease 2019 patients with respiratory failure requiring mechanical ventilation. IBW: Ideal body weight, FiO_2: Fraction of inspired oxygen, PEEP: Positive end expiratory pressure, P/F: PaO_2/FaO_2, RR: Respiratory rate, Vt: Tidal volume, SpO_2: Peripheral capillary oxygen saturation, DP: Driving pressure, Cstat: Static compliance, iNO: inhaled nitrous oxide, Pplat: Plateau pressure, ABG: Arterial blood gas, See references[56,57] for ARDSnet original sources

Table 6: Summary of key correlates with patient response to specific levels of oxygenation strategy/support

Modality	Continue HFNC Improves oxygenation and provides some added PEEP effect	Attempt awake proning for	Assisted ventilation for
Response to oxygen	Good response	Poor response	Inadequate response or increased WOB
Probable primary pathophysiology	Diffusion abnormality	V/Q mismatch	Collapsed alveoli or shunt or fragile
Caveats	Aerosolization risk	Ensure no contraindications to proning	Ensure no contraindications to NIPPV (always factor device considerations of max. FiO_2)
	Patient tolerability		

NIPPV: Noninvasive positive pressure ventilation, HFNC: High-flow nasal cannula, PEEP: Positive end expiratory pressure, WOB: Work of breathing

document; however, a dedicated Joint ACAIM-WACEM COVID-19 Clinical Management Taskforce guideline is forthcoming with recommendations specific to the implementation of home-based oxygenation strategy in patients with isolated hypoxia and clinically mild disease.

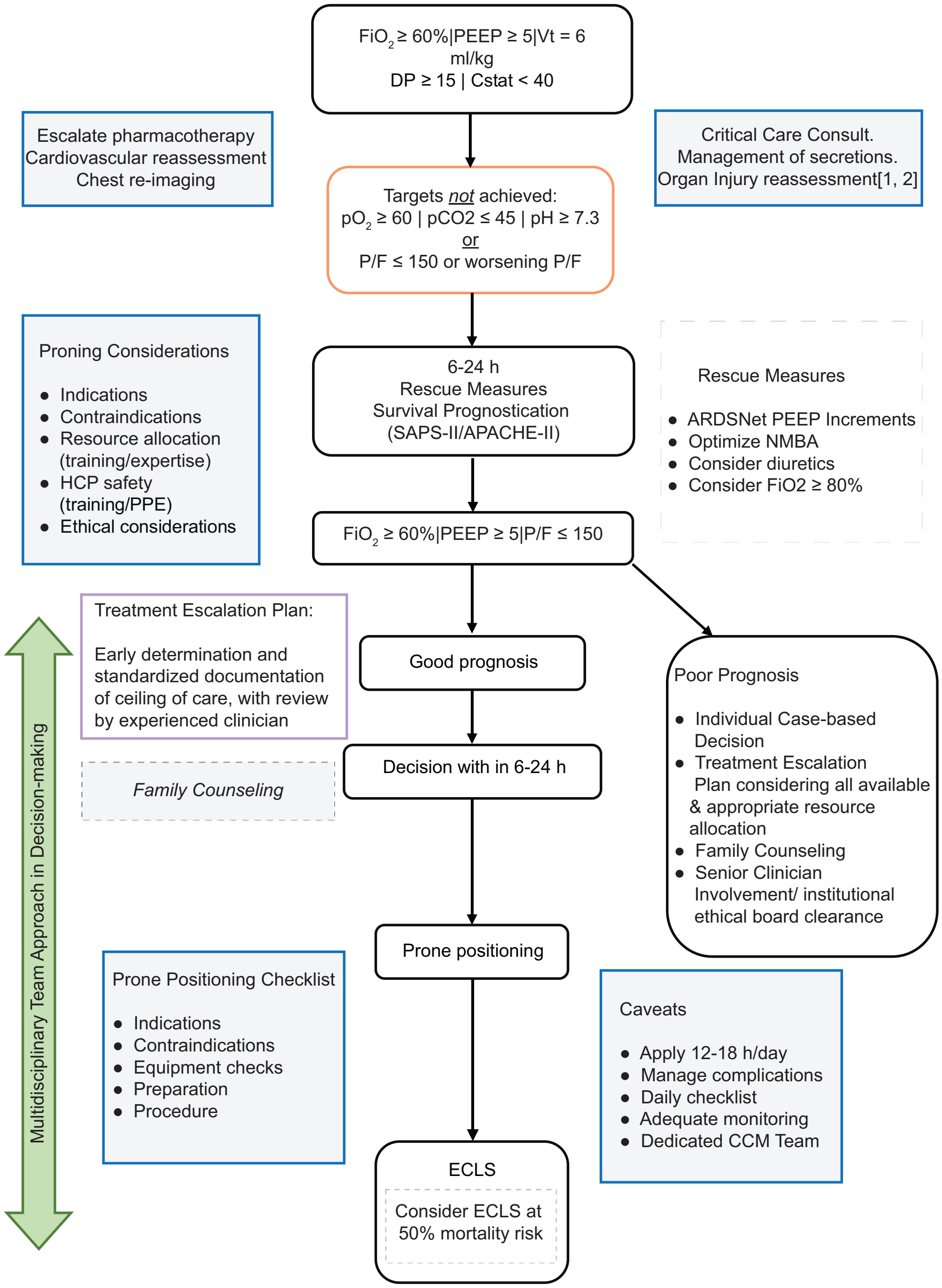

Figure 3: Management algorithm for patients with severe coronavirus disease 2019 respiratory failure. NMBA: Neuromuscular blocking agents, ECLS: Extracorporeal life support, CCM: Critical care medicine, FiO_2: Fraction of inspired oxygen, PEEP: Positive end expiratory pressure, Vt: Tidal volume, DP: Driving pressure, Cstat: Static compliance, HCP: Health-care provider, PPE: Personal protective equipment, P/F: PaO_2/FiO_2, SAPS-II: Simplified Acute Physiology score-II, APACHE-II: Acute Physiology and Chronic Health Evaluation

Table 7: Summary of important escalation points that will provide a clinically applicable framework for objective therapeutic approach transitions

Modality	Ceiling of therapy	ROX at (Hs) SpO_2/FiO_2/RR	Failure	Success
HFNC[19,20,48,49]	ROX index <3.85	2	<2.85	>4.88
		6	<3.47	>4.88
		12	<3.85	>4.88
LFNC	S/F ratio			
NIPPV	P/F ratio			
Prone	SCRB-60			
	SBC			

ROX index: Ratio of pulse oximetry/fraction of inspired oxygen to respiratory rate.[20] HFNC: High-flow nasal cannula, LFNC: Low-flow nasal cannula, NIPPV: Noninvasive positive pressure ventilation, S/F ratio: SpO_2/FiO_2, P/F ratio: PaO_2/FiO_2, SBC: Single breath count

Table 8: Summary of mechanical ventilation and proning strategies utilized in coronavirus disease-19

Ventilator strategy[13,15,50,52,54]			Proning strategy[50,51,53]	
Measure driving pressure				
Driving pressure	<15 cmH_2O	>15 cmH_2O	Indications	P/F <50 Driving pressure >15 cmH_2O Compliance <40 ml/cmH_2O
Tidal volume	8 ml/kg	6 ml/kg	Avoid if	Limited resources (PPE) Proning expertise not available
If inadequate response, consider rescue measures: NMBA, diuretic, $FiO_2 \geq 80\%$			Prerequisites	Escalate PEEP Optimize NMBA
Compliance	>40 ml/cmH_2O	<40 ml/cmH_2O	Settings	Tidal volume 6 ml/kg $FiO_2 \geq 60\%$, PEEP ≥ 5
Actions	Continue same ventilatory strategy. Proning benefit unclear	Low tidal volume High PEEP Prone positioning	Timing	Within 6 h for patients with good prognosis Within 24 h for patients with poor prognosis
Phenotype	Type L	Type H		

PPE: Personal protective equipment, NMBA: Neuromuscular blocking agents, PEEP: Positive end expiratory pressure, P/F: PaO_2/FiO_2 ratio

Table 9: Important considerations and limitations related to proning therapy

Contraindications to prone positioning[21-23,53-55]		Ceiling of therapy for (awake) prone positioning (repeated assessments every 30 min-2 h)
Absolute	**Relative**	
Unstable spine Raised ICP Thoracic or abdominal injuries	Facial injuries Morbid obesity Pregnancy	Inability to tolerate procedure Increased work of breathing (SBC, accessory muscle use) Tachypnea Hemodynamic instability Deterioration in SCRB-60 or SBC

SBC: Single breath count [Table 5], SCRB-60: Clinical risk stratification score [Table 4]

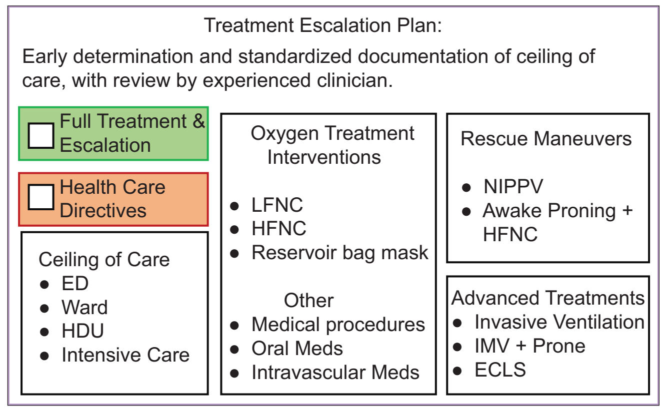

Figure 4: Treatment escalation plan checklist. ED: Emergency department, HDU: High-dependency unit, CCM: Critical care medicine, IMV: Invasive mechanical ventilation, ECLS: Extracorporeal life support, LFNC: Low-flow nasal cannula, HFNC: High-flow nasal cannula, NIPPV: Noninvasive positive pressure ventilation

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Conflicts of interest

There are no conflicts of interest.

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