NATIONAL GUIDELINE

ACUTE RESPIRATORY DISTRESS SYNDROME

Government of Nepal

Ministry of Health and Population

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Ministry of Health & Population
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Ref: .....

Date : .....3 January 2022

FOREWORD

On December 2019, the first case of COVID-19 was reported from Hubei Province of China. The Public Health Emergency of International Concern (PHEIC) was declared on 30th January, 2020 while Nepal reported its first case of COVID-19 on 23rd January 2020, a Nepalese citizen returnee from Wuhan, China. On 11th March 2020, World Health Organization (WHO) declared COVID-19 a global pandemic.

Since the first case of COVID-19 in Nepal, there has been 823,000 cases with 11,500 COVID-19 related deaths. Predominantly, COVID-19 patients are asymptomatic or only have mild symptoms; while a few may develop Acute Respiratory Distress Syndrome (ARDS), which can be life-threatening or fatal. ARDS carries a high mortality and few effective modalities exist to combat this condition.

It's my immense pleasure to express that the National Guideline for ARDS has been developed, to give proper guidance and strengthen our health system. Thus assist health workers to practice proper and ensure uniformity in diagnosis and management of ARDS. Finally, I would like to thank the technical experts and my colleagues who have actively initiated and finalized the guideline.

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FOREWORD

The development of National Guideline for Acute Respiratory Distress Syndrome (ARDS) 2021 is a result of continuous collaboration between the pool of technical experts from various specialities. This guideline being first of its kind will not only provide a uniform protocol for the diagnosis and management of ARDS but will also help in capacity building of health workers of various levels which will eventually strengthen the health system of our country. I would like to immensely thank the Government of Nepal, the technical working group and WHO Nepal for their technical support in making this possible.

The COVID-19 Unified Central Hospital, Bir Hospital, takes this opportunity to acknowledge the contribution of the following contributors.

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FOREWORD

The COVID-19 pandemic has affected various aspects of human life and put enormous pressure on the health care system and health workers. While most COVID-19 patients either have mild symptoms or asymptomatic, a few may develop Acute Respiratory Distress Syndrome (ARDS), which can be life-threatening. ARDS carries a high mortality rate and should be identified at an early stage. It is thus important to be aware of how to diagnose and effectively manage such conditions.

There have been various onsite and virtual training of health care workers across the country on management of critically ill patients with COVID-19 disease provided by Ministry of Health and Population (MoHP) with World Health Organization (WHO) support. This includes Essential Critical Care Training (ECCT), Pediatric Essential Critical Care Training (PECCT), and Infection Prevention and Control focusing on COVID-19 along with development of management guidelines for clinicians.

As COVID-19 pandemic continues, cases which develop ARDS will likewise continue to be observed. It is therefore important to have a technical guideline for ARDS which guides our health workers in providing the appropriate clinical care. To develop this essential document, MoHP formed a technical working group with experts from different professional societies involved in COVID-19 patient management with WHO Nepal support. This technical working group, led by the COVID-19 Unified Central Hospital, Bir Hospital, included intensivist, pulmonologists, critical care nurses, rehabilitation, and public health experts. The document is based on standard clinical management guideline and includes the latest, evidence-based updates on COVID-19 clinical management available globally compiled by WHO. This is the first of its kind which provides guidance in proper diagnosis and management of ARDS in Nepal, including oxygen therapy and handling critical patients in high dependency and intensive care units.

The National Guideline on Acute Respiratory Distress Syndrome will bring uniformity in early diagnosis, evaluation, and treatment of critical patients with ARDS in Nepal. It is a privilege to support MoHP in its development which will assist health workers in saving lives.

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Acknowledgement

Global pandemic of COVID-19 has emerged as a threat to whole humankind disrupting every aspect of public and curative health measures. COVID-19 has affected various aspect of human life including financial, cultural, and social norms of human civilization. COVID-19 pandemic has resulted in over 250 million cases and over 5 million confirmed deaths worldwide till date. Since the first case of COVID-19 in Nepal, there has been 823000 cases and over 11,500 COVID-19 related deaths. Severe COVID-19 pneumonia resulting into ARDS and respiratory failure is the main cause of deaths in patient with COVID-19. The knowledge of ARDS and management of respiratory failure has become a paramount importance for health care workers involved in management of COVID-19 patients. Guideline provides a consolidated guidance and a common platform for decision making in treatment and management of diseases. In the background of first and second waves in 2020 and 2021 and anticipated third wave of COVID-19 pandemic in Nepal, there was a strong need of national guideline on management of ARDS. In this aspect I would like to acknowledge and extend my gratitude to Ministry of Health and Population for providing me this opportunity to lead and draft a national guideline on ARDS. I would also like to extend my sincere thanks to World Health Organization (WHO) for providing us technical support for this task. My sincere appreciation goes to all the technical working group members; Dr. Ashesh Dhungana, Dr. Subhash Prasad Acharya, Dr. Navindra Raj Bista and Dr. Pawan Jung Rayamajhi for their contribution and inputs for drafting this guideline. My special thanks and appreciation go to Dr. Shital Adhikari (WHO consultant) for his continuous inputs, suggestion and feedback in making the outline and finalizing the content of this guideline. WHO liaison officers Dr. Deepshikha Rana and Dr. Irana Joshi have been a constant support for technical working group in compiling, drafting, and editing the contents of this guideline, my sincere thanks go to them as well.

Finally, I hope and believe this guideline will provide guidance for all health workers, doctors, nursing staffs and intensivist. I also believe this guideline would become instrumental in decision making at the bed side and patients with respiratory failure and ARDS get benefitted from this guideline. I expect and look forward to similar collaboration with MoHP and WHO in near future.

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Abbreviations

AC	Assist control
AC-PC	AC Pressure Control Ventilation
ACV	Assist control ventilation
AC-VC	AC volume ventilation
AECC	American–European consensus criteria
ALI	Acute Lung Injury
APRV	Airway pressure release ventilation
ARDS	Acute respiratory distress syndrome
ATC	Automatic tube compensation
ATS	American Thoracic Society
C	Compliance
CLABSI	Central Line Associated Blood Stream Infection
CLI	Central Line Infection
CNS	Central Nervous System
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous Positive Airway Pressure
CRBSI	Catheter-Related Blood Stream Infections
CT	Computed Tomography
DAD	Diffuse Alveolar Damage
DIC	Disseminated Intravascular Coagulation
DNE	Do Not Escalate
DNI	Do Not Intubate
DNR	Do Not Resuscitate
DP	Driving Pressure
DVT	Deep Vein Thrombosis
ECLS	Extracorporeal Life Support
ESICM	European Society of Intensive Care Medicine
ETT	Endotracheal Tube

EVLWI	Extravascular Lung Water Index
FiO_2	Fraction of Inspired Air
GCS	Glasgow Coma Scale
H_2O	Water
HFNC	High Flow Nasal Cannula
HFOV	High Frequency Oscillation Ventilation
HR	Heart Rate
I:E	Inspiration: Expiration
ICU	Intensive Care Unit
iNO	Inhaled Nitric Oxide
LDUH	Low Dose Unfractioned Heparin
LMWH	Low Molecular Weight heparin
LPM	Liters Per Minute
MIP	Maximum Inspiratory Pressure
NC	Nasal Cannula
NIPPV	Non-invasive Positive Pressure Ventilation
NIV	Non-invasive Ventilation
NMBA	Neuromuscular Blocking Agent
$PaCO_2$	Pressure of carbon dioxide
PaO_2	Pressure of Oxygen
PBW	Predicted Body Weight
PCV	Pressure controlled ventilation
PEEP	Positive end expiratory pressure
pH	Potential of Hydrogen
PIP	Peak Inspiratory Pressure
Pplat	Plateau Pressure
PSV	Pressure support ventilation
PVPI	Pulmonary Vascular Permeability Index
RASS	Richmond Agitation-Sedation Scale
RR	Respiratory Rate

S/C	Subcutaneous
SARS-CoV-2	Severe Respiratory Syndrome Corona Virus-2
SATs	Spontaneous Awakening Trails
SBT	Spontaneous Breathing Trial
SCD	Sequential compression device
SCDs	Pneumatic Sequential Compression Devices
SIMV	Synchronized intermittent mechanical ventilation
SpO2	Peripheral Oxygen saturation
SVC	Superior Vena Cava
TRALI	Transfusion related acute lung injury
UFH	Unfractioned Heparin
VA ECMO	Veno-arterial ECMO
VAP Bundle	Ventilator Associated Pneumonia Prevention Bundle
VCV	Volume Controlled Ventilation
Vt	Tidal Volume
VTE	Venous Thromboembolism
VTe	Expired Tidal Volume
VTi	Inspired Tidal Volume
V-V ECMO	Veno- Venous ECMO
WALST	Withdrawal of Active Life Supporting Treatment
ZEEP	Zero End Expiratory Pressure

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SECTION A

GENERAL

1. Introduction

Acute respiratory distress syndrome (ARDS) is an acute and life-threatening inflammatory lung injury characterized by rapidly progressing respiratory failure as evidenced by acute hypoxemia and bilateral pulmonary infiltrates. ARDS was first described in 1967 by Ashbaugh et al. as adult respiratory distress syndrome among 12 patients with bilateral lung infiltrates, respiratory failure, and severe hypoxemia. Later in 1994, a consensus between the American Thoracic Society (ATS) and the European Society of Intensive Care Medicine (ESICM) changed the term from "adult respiratory distress syndrome" to "acute respiratory distress syndrome (ARDS)'' because the syndrome occurred in both adults and children. A complex response to local and systemic inflammatory factors results into ARDS. The pathophysiological hallmark of ARDS is diffuse alveolar damage (DAD) which involves neutrophil recruitment, activation, and endothelial injury, leading to increased alveolocapillary permeability, lung inflammation and non cardiogenic pulmonary edema.

2. Definitions

In 1994, American–European Consensus Criteria (AECC) has defined ARDS as an acute onset, refractory hypoxemia with radiographic evidence of bilateral pulmonary opacities due to increased permeability of the alveolar–capillary membrane, with the exclusion of left ventricular failure as evidenced by absence of elevated pulmonary capillary wedge pressure (PAWP < 18 mm of Hg) or other evidence of left atrial hypertension.

The severity of the condition was defined by the ratio of the arterial oxygen tension (PaO_2) to the inspiratory oxygen fraction (FiO_2) i.e., PaO_2/FiO_2 ratio. Acute lung injury (ALI) was defined if the PaO_2/FiO_2 ratio is less than 300 mmHg whereas ARDS was defined if the PaO_2/FiO_2 is less than 200 mmHg. However, this definition was later modified by the Berlin definition of ARDS in 2012. In Berlin definition, the onset of ARDS is defined as within 7 days of an insult or of new or worsening respiratory symptoms. Bilateral radiographic 'opacities' are still included in Berlin definition; but other causes, such as effusions, nodules, and partial or complete collapse of a lobe or lung should be excluded before labeling as "opacities". Heart failure or fluid overload should be excluded but the methods of exclusion emphasize more on echocardiography rather than pulmonary vein catheterization and pulmonary capillary wedge pressure measurement. A minimum level of positive end-expiratory pressure (PEEP) has also been introduced in the Berlin definition of ARDS. The most striking change that Berlin definition has made is the term ALI has been omitted and in place ARDS has been graded as mild (PaO_2/FiO_2 of more than 200 mmHg but not more than 300 mmHg), moderate (PaO_2/ FiO_2 of more than 100 mmHg but not more than 200 mmHg) or severe (PaO_2/FiO_2 of not more than 100 mmHg). The major differences in AECC and Berlin definitions have been highlighted in Table 1.

Table 1: American–European Consensus Conference (AECC) and Berlin definitions of ARDS

AECC 1994	Berlin 2012
Acute onset (Time period was not specified)	Onset < 1 week of a clinical insult or new or worsening respiratory symptoms
Bilateral infiltrates in chest radiograph	Bilateral opacities on chest x-ray or CT scan of chest – after excluding effusions, lobar/ lung collapse, or nodules
PAWP less than 18 mmHg (if measured) or no clinical evidence of increased left atrial pressure	Respiratory failure not fully explained by heart failure or fluid overload. Objective assessment (e.g., echocardiography) required to exclude pulmonary edema
PEEP has not been specified	A PEEP or CPAP of ≥5 cmH2O
ALI: PaO_2/FiO_2<300 mmHg	The term ALI has been removed
ARDS: PaO_2/FiO_2<200 mmHg	Mild ARDS: PaO_2/FiO_2: 201 - 300 mmHg Moderate ARDS: PaO_2/FiO_2: 101- 200 mmHg Severe ARDS: PaO_2/FiO_2: ≤100 mmHg

3. Epidemiology

ARDS represents the common clinical problem in medical and surgical ICUs. The incidence of ARDS varies depending upon the geographic location and on the reporting system used. One of the population-based data from the United States estimated an incidence of 190,000 cases and 74,000 deaths per year from ARDS. Estimates from other prospective US cohort studies using the AECC definition range from 64.2 to 78.9 cases/100,000 person-years. Worldwide population-based incidence of ARDS ranges from 10-86 cases per 100,000 populations with highest rates being reported from Australia and USA. Incidence varies according to the geographic location, such as: Northern Europe (17 cases per 1,00,000 population), Spain (7.2 cases per 100,000 population) and New Zealand (34 cases per 100,000 population).

Mortality from ARDS has been estimated at 35% to 45%, which is an improvement from the mortality rate of 50% to 70% twenty years ago. Sepsis and multisystem organ failure are the major cause of death rather than respiratory failure alone. According to Berlin definition, increasing severity (mild, moderate, and severe) of ARDS is associated with increasing mortality (27%, 32%, and 45% respectively).

4. Etiology / Risk factors of ARDS

The common risk factors for the development of ARDS are given in Table 2. Other rare, but important treatable causes of ARDS in tropical countries include infections such as malaria, tuberculosis, enteric fever, leptospirosis, scrub typhus, heat stroke and dengue hemorrhagic fever.

Table 2: Risk factors of ARDS

AECC 1994	Berlin 2012
• Aspiration pneumonia • Fat embolism • Inhalation injury • Near-drowning • Pneumonia (Bacterial, Viral, Fungal) • Pulmonary contusion • Reperfusion injury after lung transplantation or embolectomy	• Acute pancreatitis • Amniotic fluid embolism • Cardiopulmonary bypass • Disseminated Intravascular Coagulation (DIC) • Major burns • Multiple transfusion of blood and blood products (Including TRALI)* • Neurogenic pulmonary edema • Severe trauma with shock • Sepsis

TRALI*: Transfusion related acute lung injury

Pneumonia (Aspiration and Infective) and non-pulmonary source of sepsis together account for more than 85% of ARDS cases.

5. Pathogenesis of ARDS

ARDS can be initiated by various distinct conditions that can cause direct or indirect lung injury, leading to a common uniform pathophysiological pathway of diffuse alveolar damage and capillary endothelium injury. This acute phase of ARDS is characterized by increased permeability and leakage of plasma proteins through the interstitium into the alveolar space. In turn, these plasma proteins cause activation of pro-coagulant and pro-inflammatory pathways, leading to formation of fibrinous and purulent exudates. There is increased release of pro-inflammatory cytokines such as IL-1, IL-6, IL-8 and TNF-α.

A profound acute inflammatory response is generated subsequently. This is followed by epithelial cell apoptosis and necrosis, and further activation of other inflammatory cascades, and a robust recruitment of neutrophils. The increased expression of tissue factor and other procoagulant factors ultimately leads to coagulation within the microvasculature and airspaces, accompanied by a suppression of fibrinolysis that helps the formation of microthrombi and fibrinous exudates that are pathognomonic of ARDS. This results into inflammatory vasoconstriction, decreased lung compliance and atelectasis (collapse of alveoli) due to loss of the surfactant that lines and prevents collapse of alveoli. Thus, the mechanism behind respiratory failure is severe ventilation/ perfusion mismatching with perfused alveoli not receiving any ventilation ('shunting'), while others are ventilated but not perfused ('increased dead space').

The predominant histopathology findings in all forms of ARDS are fundamentally uniform; that is "diffuse alveolar damage"- term coined by Katzenstein and colleagues in 1976 AD.

Histopathologically, there are three phases during the evolution of ARDS:

a) **An exudative early phase** typically occurs in first week and is characterized by epithelial and endothelial cell necrosis, neutrophil sequestration, platelet- fibrin thrombi, interstitial edema, and exudates within the air spaces that consist primarily of fluid, fibrin, and red blood cells which ultimately leads to diffuse alveolar damage and endothelial injury.

b) **A proliferative phase** starts from second week to fourth week; characterized by organization of the intra alveolar exudates, proliferation of type II alveolar cells and proliferation of fibroblasts.

c) **The fibrotic phase** is seen in patients who survive more than 3-4 weeks. In this phase, alveolar septa are expanded, and airspaces filled with sparsely cellular connective tissue. The chronic inflammation and fibrosis of the alveoli remodeling can progress to the point of complete air space obliteration and honeycombing.

6. COVID-19 and ARDS

The global pandemic of severe acute respiratory syndrome-corona virus-2 (SARS-CoV-2) has emerged as a threat to whole humankind, challenging the healthcare system and public health strategies worldwide with Nepal being no exception. As of November 2021, COVID-19 pandemic has resulted in over 240 million cases and over 5 million confirmed deaths worldwide. Since the first case of COVID-19 in Nepal, there has been 8,13,433 cases with 11,427 deaths and 7,92,832 recoveries till 2nd November 2021. Mortality resulting from SARS-CoV-2 infection occurs mainly through the SARS-CoV-2 induced ARDS. It is estimated that 85% of COVID-19 patients admitted in ICU meet the criteria of Berlin definition of ARDS. Elevated inflammatory cytokines (IL-6, IL-1β and TNF-α) together with impaired interferon responses, SARS-CoV-2 induced endothelial cell injury and thrombosis in pulmonary microcirculation results into severe pneumonia and ARDS in COVID-19. However clinical heterogeneity exists in COVID-19 ARDS. Gattinoni and colleagues have highlighted the heterogeneity of COVID-19 ARDS and proposed the two primary phenotypes of COVID-19 ARDS: type L (low lung elastance, pulmonary ventilation/perfusion ratio, lung weight, and low recruitability) and type H (high lung elastance, right-to-left shunt, lung weight, and high recruitability), with type H being more consistent with typical severe ARDS. Patient with COVID-19 ARDS may present early with type L and progresses into type H due to worsening of disease severity along with patient self-inflicted lung injury. The clinical course of COVID-19 ARDS follows typically one of the following three patterns: acute respiratory failure requiring immediate mechanical ventilation (type H), indolent clinical course with only moderate work of breathing (type L) or most often a biphasic course with initial indolent course followed by rapid deterioration occurring over 5-7 days. COVID-19 ARDS appears to have poor outcomes compared with ARDS from other causes or non-COVID ARDS. Overall mortality in COVID-19 ARDS ranged between 26% and 61.5%. Among COVID-19 ARDS patients who require mechanical ventilation, the mortality is even worst and can range from 65.7% to 94%.

7. Clinical Features of ARDS

The clinical presentation of ARDS can vary in intensity, depending on its cause and severity. Patient presents with severe shortness of breath, labored and unusually rapid breathing, hypotension, confusion, and extreme tiredness. These clinical features are acute on onset, occurring within

hours or days of the initial event that caused lung injury. Depending on the event that caused the ARDS, other associated symptoms can occur for example; chest pain, cough, and fever in pneumonia. Frontal chest radiograph shows extensive bilateral parenchymal and alveolar infiltrates. These infiltrates initially appear as bilateral heterogeneous opacities, but later become more homogenous over hours to days. Computed tomography (CT) of chest helps in demonstrating the distribution of ARDS which are often heterogeneous and patchy, with mixed ground-glass opacities and consolidation, often concentrated in the more gravitationally dependent regions of the lung.

8. Diagnostic Workup of a patient with ARDS

ARDS is a syndrome complex that is diagnosed using the clinical, radiological, and arterial blood gas analysis as defined by the Berlin Definition. Chest radiograph is the most performed imaging modality which reveals bilateral lung infiltrates (Figure 1a). Chest CT can supplement chest radiograph in quantification of lung edema and potential recruitability of the lung parenchyma (Figure 1b). CT can also help to distinguish ARDS from radiographic 'mimickers' like atelectasis, pleural effusions, nodules or masses. However, it may not always be feasible to transport patients with severe ARDS who are on vasoactive support and high PEEP and FiO_2 support to the CT room. In the recent years, ultrasonography is being used more commonly in the ICUs as a point of care tool for critically ill patients. Lung ultrasound in ARDS is characterized by vertical 'B lines' or 'comet-tail' artefacts, but these findings may also be present in pulmonary edema (Figure 1c). The presence of more than three 'B lines' combined with a normal cardiac echocardiography may help to distinguish ARDS from acute pulmonary edema. However, presence of heart failure does not rule out the possibility of ARDS. Lung ultrasonography can also be used to monitor lung recruitment and resolution of alveolar process. The advantages of ultrasonography are that it is inexpensive, free of ionizing radiation, portable (bed-side procedure) and easily repeatable.

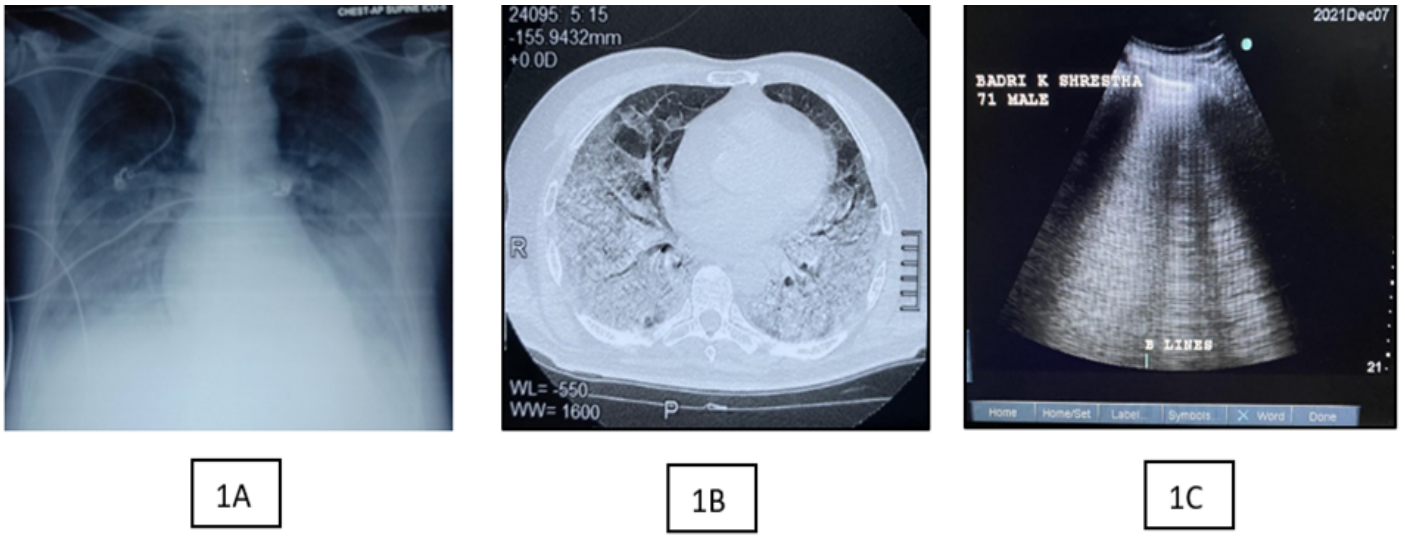


Figure 1: Radiological findings in ARDS

1A: Chest radiograph showing bilateral chest infiltrates.

1B: CT chest showing bilateral lower lobe predominant consolidation and ground glass opacities with air bronchogram.

1C: Lung ultrasound showing 'B lines' or 'Comet-tail' artefacts indicating alveolar edema.

9. Determining the Cause of ARDS

ARDS is syndrome complex that is diagnosed using the clinical, radiological, and laboratory information. Clinical history including comorbidities and travel history may provide an important clue to the inciting factor leading to ARDS. Further investigations are guided by presence or absence of inciting factors. When an obvious cause is not present, initial diagnostic workup should be directed towards the most common causes such as pneumonia or sepsis. Blood, sputum and bronchoalveolar lavage cultures aid in the diagnosis of pneumonia and sepsis. Nasopharyngeal and oropharyngeal swab for PCR for influenza and SARS Corona Virus should be sent if viral pneumonia is suspected as a cause. Bronchoscopy may aid in the diagnosis of acute eosinophilic pneumonia, alveolar hemorrhage, alveolar proteinosis and acute hypersensitivity pneumonitis as a cause. A tropical infection panel is recommended if associated findings include fever, thrombocytopenia, transaminitis or acute kidney injury. Transbronchial or an open lung biopsy is rarely considered in view of high risk of pneumothorax and bleeding.

SECTION B

MANAGEMENT

1. Respiratory Support

1.1 Oxygen Therapy

The hypoxemia in ARDS is managed with supplemental oxygen therapy, awake proning, high flow nasal cannula (HFNC), non-invasive ventilation (NIV) and Invasive ventilation or use of ECMO depending on the degree of hypoxemia and clinical condition of the patient.

Role of Supplemental Oxygen Therapy

The oxygen is one of the mainstays of supportive treatments in ARDS. The goal of the oxygen therapy is considered targeting oxygen saturation (SpO_2) and to maintain stable work of breathing.

1. Goals of therapy

a) Maintain at SpO_2 90-94%

i. However, consider SpO_2 89-92% in oxygen-dependent chronic obstructive pulmonary disease (COPD) patient

b) Maintain stable work of breathing

i. Target respiratory rate < 25 breaths/min

ii. Target normal respiratory effort (for example no use of accessory muscle or other increased respiratory effort)

2. Supplemental oxygen support

a) Start oxygen delivery via humidified nasal cannula (NC) titrated from 1 to 6 Liters per minute (LPM) to meet goals of therapy.

b) If goals of oxygen therapy are not met at 6L/min via NC then escalate to either:

i. Simple oxygen mask:

-Start at 6 LPM

-Escalate to maximum of 12 LPM to meet goals of therapy

ii. Non-Rebreather Mask (Figure 2)

- Escalate to maximum of 15 LPM (delivers FiO_2 60-80%)

iii. Venturi mask

- Start at FiO_2 40% (adjust the minimum flow rate needed to achieve 40%)
- Titrate to maximum of FiO_2 60% to meet goals of therapy

c)If goals of oxygen therapy are not met by oxygen masks or venturi mask, non-breather mask can be used while evaluating whether High flow nasal cannula (HFNC) is appropriate.

Figure 2: Non-rebreather Oxygen Mask

(PC: Dr. Shital Adhikari)

1.2 Awake Self-proning

1.2.1 Benefits of self-proning

It may improve recruitment of alveoli in dependent areas of the lungs, perfusion to ventilated areas, and V/Q matching. It is considered to decrease the differential distribution of ventilation between ventral and caudal lung portions which will shift the density distribution of edematous lung. It has been beneficial in acute hypoxemic respiratory failure.

1.2.2 Patient Selection

i. Eligibility:

- Stable patients (on room air or on supplemental oxygen) and as a "rescue" during escalation of supplemental oxygen.
- Patient should be able to move independently. They should have cognitive and physical status to supinate themselves if they feel uncomfortable.

ii. Contraindications:

1.Absolute

- Inability to independently supinate or pronate safely
- Imminent risk of intubation
- Spinal instability
- Facial or pelvic fractures
- Open chest or unstable chest wall
- Open abdomen

2. Relative contraindications

- Altered mental status
- Nausea or vomiting
- NIPPV

1.2.3 Prior to proning

- Empty the bladder
- Make plans for toileting by; call bell or cellular phone
- If possible, place the bed in reverse Trendelenburg (head above feet, 10 degrees) to help reduce intraocular pressure.

1.2.4 Prone position

- The patient should lay on his/her abdomen (arms at sides or in "swimmer" position).
- A pillow placed under the hips and/or shoulders may help for comfort.
- If difficulty to tolerate, they may rotate to lateral decubitus or partially prop to the side (in between proning and lateral decubitus) with the use pillows or cushion as required.

1.2.5 Proning Time

- Patient should try proning every 4 hrs. and stay prone for as long as tolerated. Proning is often limited by patient discomfort, but the patient should be encouraged to reach achievable goals, like 1-2 hours (or as long as possible).
- Patient should attempt to prone at night as tolerated.

1.2.6 When to stop awake proning

- Patient can stop self-proning at any time
- If intubation is being considered
- If the patient doesn't require supplemental oxygen or improved for home discharge

1.3 High Flow Nasal Cannula (HFNC)

a. HFNC improves hypoxemia and reduces the work of breathing or dsypnea.

b. Severe work of breathing is a relative contraindication for HFNC.

c. Heated and humidified oxygen should be used.

d. Start flow rate with 30L/min and increase it if it benefits the patient. Flow rate up to 60L/min can be considered.

e. Frequent assessment should be done to assure HFNC is medically indicated, or if condition is worsening where patient might benefit from intubation. Considerations should be taken such as:

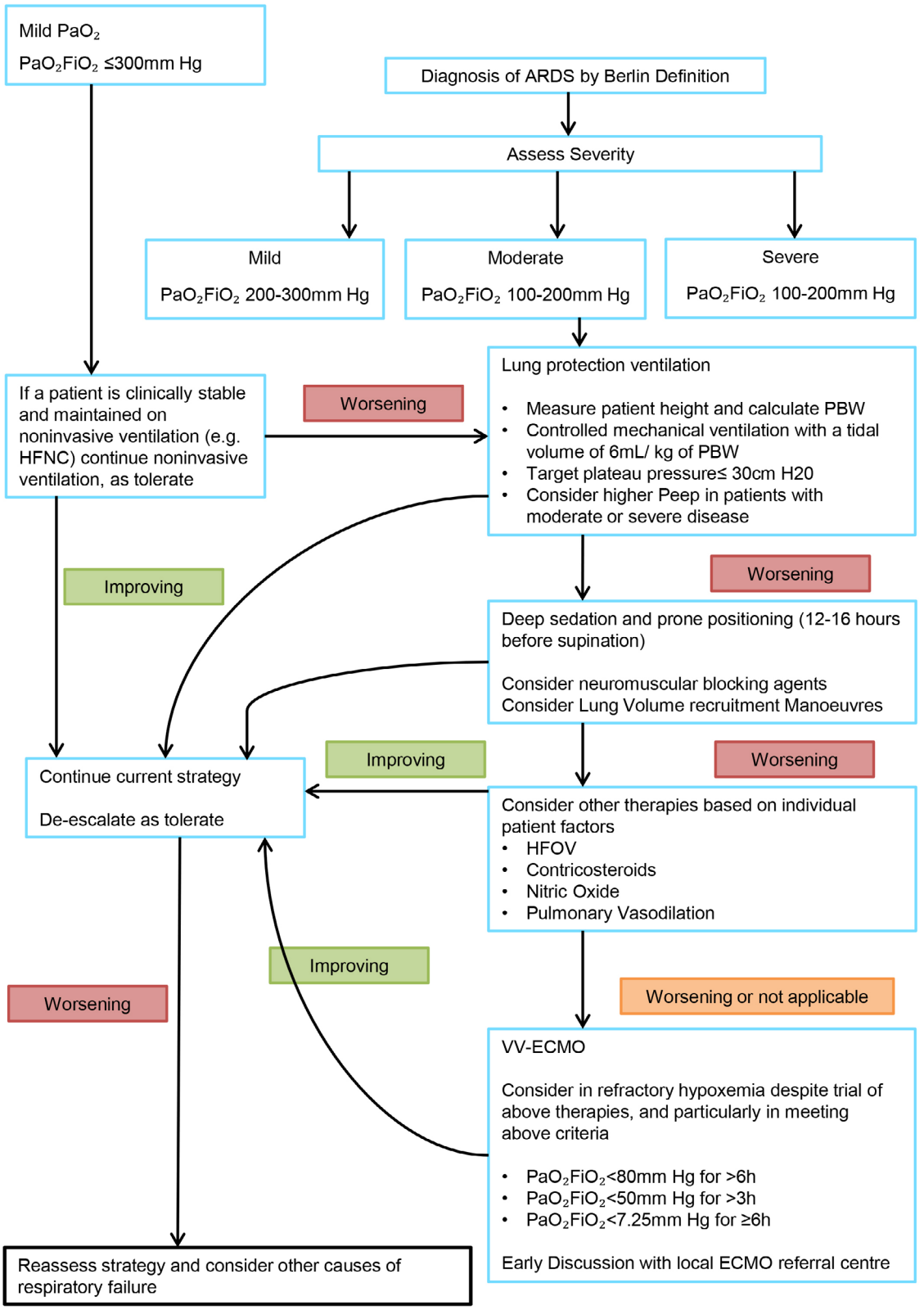
i. Is there concern for the work of breathing? (use of accessory muscles, difficulty in speaking, tachypnea)

ii. Is there concern for volutrauma or barotrauma that could worsen ARDS?

iii. Is HFNC meeting the patient's oxygenation goals?

iv. Other considerations during oxygen support escalation:

- Encourage awake self-proning if no contra-indications.
- Awake self-proning signifies that the patient can self-supinate independently.
- Self-proning can be done while the patient is on HFNC if the patient meets all self-proning criteria.



Flowchart 1: Treatment algorithm for Acute Respiratory Distress Syndrome (ARDS)

1.4 Ventilatory Management

The goals of respiratory support with mechanical ventilation in patients with ARDS using a lung protective strategy is to improve survival and to prevent complications.

1.4.1 Basics of Mechanical Ventilation

Mechanical ventilators are devices used to improve oxygenation and carbon dioxide removal. This can be done invasively by inserting endotracheal tube into trachea or tracheostomy or non-invasively by using different interfaces like face mask or nasal cannula or helmet. The aims of mechanical ventilation are one of the following:

i. Improve oxygenation
ii. Improve ventilation (CO_2 removal)
iii. Decrease work of breathing
iv. Replace respiratory drive due to central nervous dysfunction

First, few terminologies will be described.

1. Tidal volume (VT): It is the amount of fresh air pushed into the alveoli with each breath. Inspired tidal volume is called VTi and exhaled tidal volume is VTe.

2. Minute ventilation (MV): It is amount of inspired or exhaled air in a minute. It depends on tidal volume and respiratory rate (VT x RR). Removal of carbon dioxide depends on minute ventilation.

3. Fraction of inspired oxygen (FiO_2): It is the fraction of oxygen in inspired air.

4. Positive end-expiratory pressure (PEEP): It is the pressure above atmospheric pressure added through the ventilatory circuit (via a pressure-sensitive valve in the expiratory limb of the circuit). It increases the end-expiratory or baseline airway pressure to a value greater than atmospheric pressure (0mmHg). PEEP is used routinely during mechanical ventilation to open collapsed alveoli (recruitment) and to prevent the collapse of distal airspaces at the end of expiration.

5. Compliance: It describes the elastic properties of lungs and chest wall and indicates the ease of distension of alveoli. Mathematically, it is change in volume per unit change in pressure.

$C=\Delta V/\Delta P$ where C is the compliance in L/cm H_2O, ΔV is the change in volume and ΔP is change in pressure.

If compliance is decreased increased pressure is needed to deliver the required tidal volume. Patients with low compliant lungs often have a restrictive type of lung defect: low lung volumes, and low minute ventilation. In ARDS, lung compliance can be low i.e., the lungs are stiff, and the work of breathing is increased.

6. Airway resistance: It is the resistance to gas flow into the airways during inspiration. It can be measured by dividing the pressure drop between mouth and alveoli by the flow rate. In the spontaneously breathing adult, it is 2-3cm H_2O/L per sec. When an ET tube / tracheostomy tube is placed, the diameter will be smaller than the normal airway and resistance to flow increases to about 6cm H_2O/L per sec. The resistance of a tube varies inversely as the fourth power of the radius of the tube.

In critically ill patient on mechanical ventilator, changes in compliance and resistance may occur. When lung compliance is decreased, there will be increase in airway pressure in volume-controlled mode, and in pressure-controlled ventilation, tidal volume decreases.

7. Airway pressure: All airway pressures are measured in cm water (cm H_2O) relative to atmospheric pressure which is taken as zero. Pressure is measured at different phases of respiration.

a. Peak inspiratory pressure (PIP): It is the highest pressure during the inspiratory phase. The peak pressure depends on the following:

i. Lung-chest wall compliance
ii. Airway resistance
iii. Delivered tidal volume
iv. Inspiratory flow rate
v. End expiratory pressure (PEEP)

b. Plateau pressure (Pplat): It is the airway pressure when the inspired gas redistributes to peripheral airways and alveoli. It is measured by pressing the button inspiratory pause. It reflects the elastic recoil pressure of the lungs and thoracic cage. Low compliance results in an elevated plateau pressure. The plateau pressure provides the best approximation of the transalveolar pressure.

c. Driving pressure (DP): It is the difference between plateau pressure and positive end-expiratory pressure (Pplat-PEEP) and can also be expressed as the ratio of tidal volume to respiratory-system compliance (VT/CRS).

Driving pressure is most strongly associated with mortality and target is to keep below 13–15cm H_2O. It represents the stress applied to the lungs and adjusting tidal volume according to driving pressure rather than to predicted body weight may lead to better outcomes for patients, especially those with severely injured lungs.

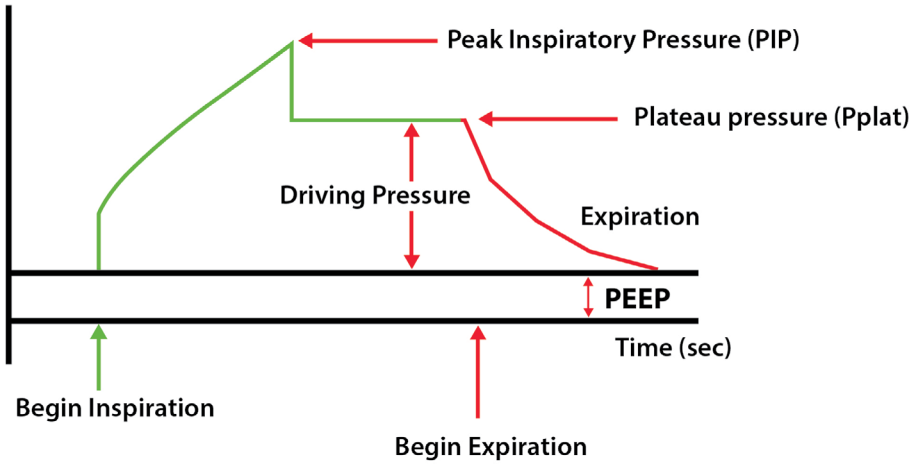


Figure 3: Components of Inflation Pressure

Ventilation parameters

Ventilation parameters can be broadly grouped into:

I. Control variables
II. Phase variables
III. Conditional variables

I. Control variables

When providing ventilatory support, the mechanical ventilator can control four primary variables during inspiration: pressure, volume, flow, and time.

1.Pressure

A pressure greater than atmospheric pressure is applied to the lungs, causing them to expand and

deliver tidal volume. Once positive pressure is no longer applied, the patient exhales passively to ambient pressure. Exhalation occurs because of the pressure differential between the lungs and the atmosphere caused by the elastic recoil of the lungs and thorax. The pressure level that is delivered to the patient will not vary despite changes in patient compliance or resistance.

2.Volume or flow

In volume-controlled ventilation, tidal volume is preselected and the pressure in the airways rises steadily until the preselected volume is delivered. Even though a tidal volume is set or displayed, many ventilators measure flow and then derive volume from the flow measurement.

Volume (L)= Flow (L/sec) x Inspiratory Time (sec)

3.Time

The time can be controlled for maintaining the set pressure for a prescribed time or for adjusting the tidal volume at a set flow rate. When considered along with the set respiratory rate, it determines the inspiratory and expiratory time (I: E) ratio.

Ventilator can control only one variable at a time: pressure, volume, or flow. Because volume and flow are inverse functions of one another, we can consider only pressure and volume as control variables.

II. Phase variables

A ventilator-supported breath may be divided into four distinct phases:

1. Initiation of inspiration (trigger)
2. Inflation phase (Inspiration)
3. Cycle to exhalation (cycling)
4. Exhalation

Each phase is described briefly.

1. Initiation of inspiration (trigger)

Inspiration can be started by patient effort, patient triggering, after a predetermined time, time triggering and manually, manual triggering.

a. Patient triggering: This can be based on pressure or flow.

i. Pressure trigger

The ventilator senses the patient's inspiratory effort as a drop in baseline pressure (or end expiratory pressure) when patient attempts to inhale. The sensitivity is set as -2 to -4 cm H_2O. For example, if the sensitivity for pressure triggering is set at -2 cm H_2O, then the patient must generate a pressure of -2 cm H_2O at the airway opening to trigger the ventilator into inspiration. If auto-PEEP is present (described later) the patient must overcome both the auto-PEEP level and the sensitivity setting. Figure: pressure trigger mechanism.

ii. Flow trigger

A continuous flow passes through the ventilator circuit and returns to the ventilator (i.e., delivered flow = returned flow). As the patient initiates a breath, part of the delivered flow goes to the patient and the return flow to the ventilator is therefore reduced (i.e., delivered flow> return flow). The ventilator senses this reduced flow and initiates inspiration. Flow triggering reduces work of breathing as compared to pressure triggering.

b. Time triggering: Time-triggered breath is initiated and delivered by the ventilator as per preset time. If respiratory rate is set 15 breaths per minute (60 sec), time triggering interval is 4 seconds (60/15= 4). The entilator delivers one mechanical breath every 5 sec without patient's breathing effort or requirement. It is used in fully controlled ventilation or back up safety system in case the patient fails to trigger inspiration.

c. Manual triggering: It is used to manually ventilate the patient prior to suctioning and in emergency.

2. Inflation phase (Inspiration)

a. If tidal volume is set directly, the machine sets the flow and time automatically depending on the set respiratory rate (RR) and I: E ratio.

If VT is set 400 ml (0.4 L), RR= 10 breaths/minute and I: E= 1:2. Each respiratory cycle is of 6 seconds and inspiratory time is 2 seconds. Then the flow will be

Flow=VT/2= 0.4/2=0.2L/seconds= 0.2x60 L/min= 12L/minute

The pressure is automatically achieved depending upon lung compliance. If pressure limit is set low and lung compliance is reduced, the set volume will not be delivered.

b. If pressure is set directly, the duration of inspiration is time limited. Tidal volume varies.

c. In some ventilators, flow rate and inspiratory time (determine tidal volume) is directly set along with inspiratory pause and expiratory time. Tidal volume depends on flow rate and inspiratory time whereas total inspiratory time, inspiratory pause and expiratory time determine respiratory rate.

d. Inspiratory to expiratory time ratio (I: E ratio)
I: E ratio depends upon respiratory rate, flow and set inspiratory time. Decreasing the respiratory rate with fixed inspiratory time will increase the expiratory time. Increasing flow will decrease the inspiratory time. Normally, it is set 1:2 but may need to increase the inspiratory time in ARDS patient to improve oxygenation.

3. Cycle to exhalation (Cycling)

The inspiratory phase always ends when some variable reaches a preset value. The variable that is measured and used to end inspiration is called the cycle variable.
Cycling could be volume, pressure, flow, or time.

a. In volume cycling, inspiratory phase ends when preset tidal volume is delivered.

b. In pressure cycling, inspiratory phase ends when pressure reaches the preset value.

c. Flow cycling, the most frequent application of flow cycling is in the pressure-support mode. In this mode, the control variable is pressure, and the ventilator provides the flow necessary to meet the inspiratory pressure target. Flow starts out at a relatively high value and decays exponentially. Once flow has decreased to a relatively low value (such as 25% of peak flow, typically preset by the manufacturer), inspiration is cycled off.

d. In time cycling, inspiratory phase ends when preset time is completed.

4. Exhalation

Exhalation is a passive process. Intrapleural pressure during exhalation can be equal to atmospheric pressure, which is called zero end expiratory pressure (ZEEP) or it can be above atmospheric pressure called positive end expiratory pressure (PEEP). PEEP is commonly used in ventilators which facilitate exhalation by splinting the airways open and reducing airway collapse. It has been recommended that at least 3-5cm H_2O of PEEP (physiological PEEP) be used in all patients with endotracheal tube / tracheostomy to prevent alveolar collapse (where the normal glottic closure is bypassed).

Beneficial effects of PEEP

a. Improve oxygenation by:

i. Increasing functional residual capacity

ii. Increasing alveolar volume

b. Improve lung compliance by

i. Alveolar recruitment

ii. Decreased venous return due to increased intrathoracic pressure (useful in congestive heart failure)

c. Reduce dead space by recruitment of collapsed alveoli and recruitment

d. Reduce work of breathing due to alveolar recruitment

e. Improve in cardiac output especially in patients with congestive heart failure

Deleterious effects of PEEP

a. Barotrauma due to overdistension of alveoli

b. Organ perfusion:

i. Cerebral - PEEP increases cerebral venous pressures and can increase ICP.

ii. Renal- ADH levels increase (in response to reduced venous return to the heart) and causes a reduction in urine output.

iii. Hepatic - Elevated intrathoracic pressure can impede hepatic venous return and perfusion causing hepatic congestion.

iv. Cardiovascular- PEEP can cause hypotension especially in patient with hypovolemia due to decreased venous return.

Levels of PEEP depends upon underlying lung condition and disease process. For ARDS patient, it is described later in the ventilator settings.

Auto-PEEP

Auto-PEEP (intrinsic PEEP, inadvertent PEEP, occult PEEP) is the unintentional PEEP during mechanical ventilation due to incomplete alveolar emptying during expiration resulting in a dynamic hyperinflation (air trapping).

The common scenarios are :

a. Abnormal respiratory mechanics, e.g., obstructive airway diseases.

b. Inappropriate ventilator settings (e.g., high respiratory rate (>20 breaths/ minute), inadequate expiratory time due to low inspiratory flow rates, and relatively equal (about 1:1) or inversed I: E ratio.

Auto-PEEP is described in the section of troubleshooting.

III. Conditional variables: modes of ventilation

It refers to the pattern of interaction between the machine and the patient. A few terminologies are used.

1. Spontaneous breath is initiated and terminated by the patient. When inspiratory pressure is applied to spontaneous breath, it is called supported breath.

2. Mandatory breath: Time triggered breaths and patient triggered breaths in which the control and phase variables are regulated by the machine are all considered mandatory breaths. A mandatory breath which is patient triggered is termed assisted breath.

3. Spontaneous ventilation: Both rate and tidal volume are controlled by the patient.

4. Controlled Mandatory Ventilation (CMV): All breaths are mandatory breaths and there is no mechanism for patient triggering (if patients can trigger, it becomes Assist Control). The rate and tidal volume are controlled by the machine. It can be given as volume control or as pressure control. CMV is used for patients who are unconscious or whose respiratory muscles are paralyzed.

5. Assisted ventilation: The rate is controlled by the patient, but the tidal volume is assisted by a set pressure given as support for every triggered breath (inspiratory pressure support). In practice, the pressure support is set at a level which delivers a tidal volume of adequate amount to maintain the spontaneous respiratory rate below 30/minute. This mode is not used in its pure form by itself - if the patient fails to trigger the machine, will result a dangerous apnea. There is always a backup mode if assist ventilation is used - assist-control.

6. Pressure Support Ventilation (PSV) is pressure-augmented spontaneous breathing. It differs from patient-triggered PCV because it allows the patient to terminate the lung inflation, whereas the ventilator terminates the lung inflation during patient-triggered PCV. Therefore, PSV is a more interactive form of ventilation than PCV because it allows the patient to control the inspiratory time and tidal volume. PSV uses a decelerating inspiratory flow rate, with high flow rates early in inspiration to achieve the desired pressure level. The pressure-augmented breath is terminated when the inspiratory flow rate falls to 25% of the peak level. This allows the patient to determine the duration of lung inflation and the tidal volume.

In summary, in PSV mode a preset pressure-assisted breath is triggered by the patient's own inspiratory effort. Patient breathes spontaneously and determines rate; VT is determined by inflation pressure used and patient's lung-thorax compliance.

7. Assist-Control Ventilation (ACV): It allows the patient to initiate a ventilator breath (assisted or patient-triggered ventilation), but if this is not possible, ventilator breaths are delivered at a preselected rate (controlled or time-triggered ventilation). The ventilator breaths during ACV can be volume-controlled or pressure-controlled. A set tidal volume (if set to volume control; AC-VC) or a set pressure and time (if set to pressure control; AC-PC) is delivered at a minimum rate. Additional ventilator breaths are given if triggered by the patient which are assisted to the level preset (volume or pressure).

8. Synchronized Intermittent Mechanical Ventilation (SIMV) with pressure support: This mode is designed to allow spontaneous breathing between ventilator breaths, the ventilator breath is delivered in synchrony with the spontaneous breath. The ventilator breaths during SIMV can be volume-controlled or pressure-controlled. The rate of ventilator breaths is adjusted as needed to match the total minute ventilation (spontaneous plus assisted breaths) to the patient's baseline level. To assist the spontaneous breath, inspiratory pressure support is applied.

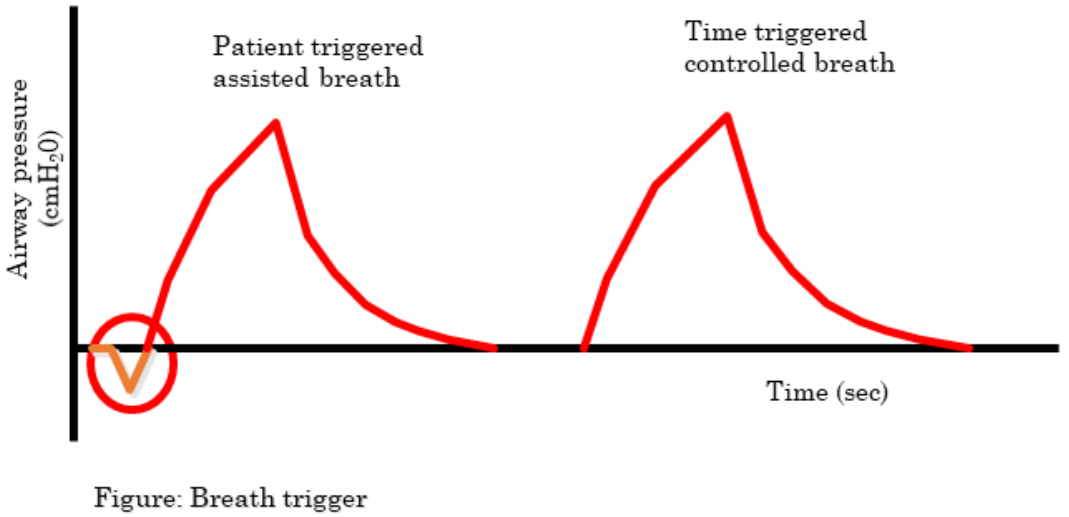


Figure: Breath trigger

Figure 4: Pressure-Time Scaler showing patient triggered and time triggered controlled breath

This mode allows patients to assume a portion of their ventilatory drive but usually associated with greater work of breathing than assist controlled ventilation and therefore is less frequently used ventilator mode. Like AC SIMV can be-volume control or pressure control.

Table 3: Advantages and disadvantages of different modes of mechanical ventilation

Mode	Advantages	Disadvantages
Assist control ventilation (AC): AC-VC/AC-PC	Reduced work of breathing	Potential adverse hemodynamic effects and hyperventilation
AC volume ventilation (AC-VC)	Guarantees set tidal volume	May lead to excessive inspiratory pressure
AC pressure control ventilation (AC-PC)	Allows limitation of peak inspiratory pressure (PIP)	Potential hyper- or hypoventilation with lung resistance/ compliance changes
Pressure support ventilation (PSV)	Patient comfort, improved patient ventilator interaction	Apnea alarm is only back-up, variable patient tolerance
Synchronized Intermittent Mandatory Ventilation (SIMV)	Less interference with normal cardiovascular function	Increased work of breathing compared to AC

Table 4: Summary of the modes of ventilation

Mode	Trigger	Limit	Cycle
Volume controlled	Time	Volume	Time/ volume
Pressure controlled	Time	Pressure	Time
Volume controlled, assist-controlled	Time/flow/pressure	Volume	Time/ volume
Pressure controlled, assist-controlled	Time/flow/pressure	Pressure	Time/ volume
Synchronized intermit-tent mandatory	Time/flow/pressure	Volume	Time/ volume
Pressure support	Pressure/flow	Pressure	Time/ volume

Primary goals of mechanical ventilation are:

a. Adequate oxygenation/ventilation

b. Reduced work of breathing

c. Synchrony of ventilator and patient, and avoidance of high peak pressure

Effects of mechanical ventilation (positive pressure ventilation)

Advantages

1. Reduction of work of breathing
2. Ability to ventilate despite adverse changes in compliance and/or resistance
3. Presence of endotracheal tube (ET tube)/tracheostomy tube allows maintenance of bronchial hygiene

Complications of Mechanical ventilation

Complications of mechanical ventilation can be due to endotracheal tube positioning or patency, positive pressure, and ventilator settings.

1. Cuff related: aspiration, cuff leaks, tracheal necrosis.
2. Infection: ventilator associated pneumonia
3. Positive pressure related:
    a. Barotrauma
    b. Intrinsic or auto PEEP
    c. Volutrauma
    d. Biotrauma
    e. Decreased cardiac output, cerebral, renal, and gastrointestinal perfusion
4. Equipment malfunction, incorrect use, wrong setting.
5. Psychosis, suffering, pain, discomfort
6. Oxygen toxicity, absorption atelectasis

1.4.2 Protocol for Use of Neuromuscular Blocking Agents (NMBA)

• Avoid continuous sedation and neuromuscular blockade when possible.

• If NMBA must be used in ICU, it MUST always be used in conjunction with sedatives like Fentanyl/Morphine.

• NMBA must be used ONLY in following conditions in ICU:

  o During Intubation

  o In intubated patients during Bronchoscopy or other procedure

  o Patient ventilator dyssynchrony: In mechanically ventilated patients when there is patient ventilator dyssynchrony even with adequate sedatives (RASS more than – 2), and not able to manage dyssynchrony, 1-2 doses of intermittent boluses of neuromuscular blocking agents can be given. If persistent dyssynchrony, high plateau pressures or if prone ventilation then continuous NMBA may be needed for up to 24 hrs

  o In Refractory Hypoxia or Severe ARDS, only during first 24 - 48 hours

I. Drugs used for NMB in ICU

1. Atracurium

• Commonly used NMBA for Intubation, Dyssynchrony and for procedures in ICU

• Bolus Dose: 0.4-0.5 mg/kg IV bolus

• Continuous infusion: 0.005-0.01 mg/kg/min IV

• Dose adjustment not necessary in renal and hepatic impairment

• Onset: 2-3 min; may be slightly delayed in patients with renal failure

• Duration of action: 20-35 min

2. Cisatracurium

• NMBA recommended for use in severe ARDS for initial 24-48 hours as continuous infusion

• Bolus Dose: 0.15-0.2 mg/kg IV bolus

• Continuous Infusion: 1-3 mcg/kg/min

• Renal and Hepatic impairment doesn't require dose adjustment due to degradation by Hoffman's degradation, but in prolonged infusion monitoring is required as the metabolite (Laudanosine) can cause seizure

3. Rocuronium

• Fast onset makes Rocuronium suitable drug for Rapid Sequence Induction and Intubation

• Dose for Rapid Sequence Intubation 0.6-1.2 mg/kg IV

• Dose for Regular Intubation: 0.5-0.6 mg/kg IV

• Continuous infusion: 0.01-0.012 mg/kg/min IV

• Duration of action: 30-60 minutes (0.6 mg/kg – 1.2 mg/kg)

All other NMBA and Muscle Relaxants MUST NOT be used in ICU because of their adverse effect profiles and increased incidence of ICU Acquired Weakness.

1.4.3 Lung Protective Ventilation

Supportive therapy for ARDS is focused on limiting further lung injury through a combination of lung-protective ventilation to prevent ventilator associated lung injury and conservative fluid therapy to prevent lung edema. The optimal approach is still unknown but low tidal volume (6 ml/Kg predicted body weight) and limiting plateau pressure (< 30 cm H_2O) were found to improve survival, shortened duration of mechanical ventilation, and reduce the incidence of extra-pulmonary organ failure. Because the volume of aerated lung is reduced in patients with ARDS, even normal tidal volumes delivered with airway pressures that are considered safe for the uninjured lung may cause regional over distention (volutrauma), atelectrauma (repeatative opening and closing of lung units and biotrauma (epithelial and endothelial injury resulting in translocation of inflammatory mediators and bacterial products). Limiting the driving pressure below 15cm H_2O (plateau pressure-PEEP) which represents the tidal volume corrected for patient's respiratory compliance is being used to limit the volutrauma and improve survival. This section describes the different ventilator strategies used in ARDS patients.

I. Ventilator settings for ARDS

1. Low tidal volume

A tidal volume around 6 mL/kg of predicted body weight (PBW) should be used as a first approach in patients with recognized ARDS, in the absence of severe metabolic acidosis, including those with mild ARDS, to reduce mortality. The adjustment of tidal volume between 4-8 ml/Kg PBW to keep plateau pressure below 30 cm H_2O allowing permissive hypercapnia.
(strong recommendation)

PBW for men =50 + 2.3 (height in inches – 60)

PBW for women = 45+2.3 (height in inches – 60)

Once tidal volume is set to around 6 mL/kg PBW, plateau pressure should be monitored not allowing it to exceed 30 cm H_2O. Volume or pressure-controlled mode can be used (described later).

If the plateau pressure is >30 cm H_2O, then tidal volume should be lowered to 5 mL/kg or as low as 4 mL/kg, if needed. The only way to monitor plateau pressure is to ventilate the patient with an end-inspiratory pause, a pause of 0.2–0.3 sec.

Volume-controlled or pressure-controlled mode of ventilation

It is unlikely that mode of ventilation influenced the outcome in ARDS since flow, driving pressure, and frequency determine the power, and the factor by which ventilation injures the lungs, it seems unlikely that the way this power is delivered (i.e., flow pattern) plays a major role. A meta-analysis of 3 RCTs found a relative risk of hospital and ICU mortality for pressure-controlled ventilation (PCV) versus volume-controlled ventilation (VCV) of 0.83 (95 % CI 0.67–1.02; p = 0.08) and 0.84 (95 % CI 0.71–0.99; p = 0.04), respectively.

Permissive hypercapnia

A subset of patients may develop high partial pressure of carbon dioxide ($PaCO_2$) when lung protective ventilation with low tidal volume is used in ARDS. Severe hypercapnia has deleterious effects such as renal and cardiovascular dysfunction and increased mortality. Current evidence suggests maintaining $PaCO_2$ < 50 mmHg. An arterial pH of 7.30 to 7.45 is desirable but some patients may tolerate arterial pH as low as 7.15.

Strategies to reduce hypercapnia

Unintended hypercapnia in patients with ARDS when using lung protective ventilation may be the result of higher dead space associated with increasing disease severity. It is important to identify early in the disease process.

These are the strategies are useful though complex to reduce hypercapnia.

1. Reducing alveolar dead space with adequate lung recruitment to facilitate in ARDS with optimal PEEP level avoiding over distension.

2. Second, titrating PEEP and driving pressure to achieve a desired tidal volume and PaCO2 threshold.

3. Increasing respiratory rates to increase minute ventilation to correct hypercapnia is an option but are not tolerated in some patients with dynamic hyperinflation and right ventricular dysfunction.

In summary, strategies to lower PaCO2 can be associated with significant harm, and their use must be weighed against the risks associated with permissive hypercapnia.

2. Respiratory rate

Though the occurrence of ventilator induced lung injury (VILI) or outcome in ARDS has not been independently studied, lung injury may be related to the frequency of repetitive collapse and expansion. The degree of tissue damage probably depends on the pressure amplitude rather than frequency, but higher respiratory rate reduces expiratory time and may cause auto-PEEP.

3. Inspiratory, expiratory ratio (I: E)

Increasing inspiratory time has been found to improve oxygenation. The effect of a high I: E ratio in hypoxemic ARDS patients is related to the resultant increase in

a. Intrinsic PEEP (PEEPi),

b. Improved ventilation of units with long time constants, and

c. Alveolar recruitment secondary to increased mean airway pressure (MAP)

The clinical outcomes of different I: E ratios are conflicting but using PEEP is probably more physiological approach than increasing inspiratory time.

4. PEEP

A PEEP of at least 5 cm of water is recommended.

Adjusting PEEP or tidal volume to minimize driving pressure (the difference between plateau airway pressure and PEEP) is also rational, since with this approach, the tidal volume is adjusted in proportion to the patient's respiratory system compliance (to avoid over distention). Adjusting the PEEP to minimize driving pressure may align the PEEP with the best respiratory system compliance, thus balancing the opening of the lung (and preventing atelectrauma) against over distention (limiting volutrauma).

Ventilatory settings II: PEEP/ recruitment

The application of PEEP in ARDS patient is to improve oxygenation and prevent ventilator induced lung injury by minimizing tidal alveolar opening and collapse (atelectrauma). The role of alveolar recruitment in clinical outcomes remains controversial. A meta-analysis found that use of higher PEEP could improve survival though the diagnosis of ARDS was PaO_2:FiO_2 < 200 mmHg.

To summarize the PEEP in ARDS

a. PEEP is an essential component of the management of ARDS and the experts suggest using a value above 5 cm H_2O in all patients presenting with ARDS.

b. The PEEP level commonly set is based on ARDS net protocol.

Table 5: PEEP table

Lower PEEP/higher FiO_2

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7
PEEP	5	5	8	8	10	10	10	12

FiO_2	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	14	14	14	16	18	18-24

Higher PEEP/lower FiO_2

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5
PEEP	5	8	10	12	14	14	16	16

FiO_2	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	18	20	22	22	22	24

c. PEEP settings should be individualized reserving high PEEP for patients in whom it improves oxygenation without marked deterioration of respiratory system compliance or hemodynamic status. The physiologic parameters such as respiratory system compliance, oxygenation, and driving pressure are commonly used to decide optimal PEEP. Other parameters that can be used for PEEP titration are transpulmonary pressure (esophageal monitoring) and CT scan and electrical impedance tomography.

5. FiO_2 should be titrated to achieve target oxygen saturation (SpO_2 90-92% or $PaO_2 \geq 60$ mmHg).

Evaluation of ARDS management

The efficacy and safety of all ventilation parameters and therapeutics associated with ARDS management should be evaluated at least every 24h (expert opinion).

1.4.4 Prone Position Ventilation

Prone position has been used since 1970 as a method to improve oxygenation but this physiological improvement was found to improve survival of patients with severe ARDS patients only in 2013 in Proning Severe ARDS Patients (PROSEVA) trial. Subsequent meta-analysis also showed prone positioning as an effective way to reduce mortality in patients with moderate to severe ARDS when used with other lung protective strategies. In the COVID-19 pandemic, prone positioning has been adopted even before intubation popularly termed as awake prone positioning. This section describes the rational of prone positioning and practical applications in ARDS.

Effects of prone position on lung/chest wall compliance, ventilation, and gas exchange:

I. Chest wall compliance

For anatomical reasons, the posterior chest wall (including spine and the scapulae) is less compliant than the anterior component (sternum and ribs). In the prone position, the bed surface impedes expansion of the anterior structures while abdominal compliance remains relatively unmodified. So, there will be a decrease in overall chest wall compliance in prone position.

II. Lung compliance

In ARDS patients, lung compliance is primarily determined by the number of opening pulmonary units. In the prone position a favorable shift may result from promoting the homogeneous distribution of total stress and strain. When a person is supine, the weight of the edematous lungs, heart, and abdominal viscera increase dorsal pleural pressure which reduces transpulmonary pressure (airway opening pressure– pleural pressure) in the dorsal lung regions. Placing a person in the prone position reduces the pleural pressure gradient from nondependent to dependent regions, in part through gravitational effects and conformational shape matching of the lung to the chest cavity with more equitable aeration distribution. The benefits are:

a. More uniform distribution of pleural and plateau pressure

b. More uniform compliance

c. Less cyclical atelectasis and alveolar overdistension

d. Perfusion and ventilation: alveolar recruitment is better in prone position because this position reduces the difference between the dorsal and ventral pleural pressure, and the compliance is more homogenous. Studies have found that prone positioning improves oxygenation in most patients with ARDS (70%-80%), and the average ratio of PaO_2/FiO_2 is increased by 35 mm Hg.

e. The dorsoventral orientation of larger airways enhances the drainage of secretions when patient is in prone position.
The prone position generally improves oxygenation, but its ability to limit mechanical lung injury may be the more important mechanism of clinical benefit.

Clinical indications

a. Patients with ARDS when $PaO_2/FiO_2 < 150$ mm Hg)

b. Early in the course (ideally within 12-24 hours of stabilization)

Lung protective ventilation strategies should be used simultaneously.

Contraindications

a. Open abdomen, wounds or burns over the ventral body surface

b. Facial/neck trauma or spinal instability

c. Patients with elevated intracranial pressure

d. Patients with massive hemoptysis

e. Patients at high risk of requiring CPR or defibrillation

Limitations and potential complications of prone positioning

i. Increase nursing overload

ii. Dislodgement/kinking of tubes including ET tube

iii. Pressure sores: eyes, lips, bridge nose, shoulder etc.

iv. Implement at bed side

v. Temporary increase in oral and tracheal secretions (may cause airway obstruction)

vi. Raised intracranial and intrabdominal pressure

Prone positioning

It requires 3-5 people, close attention to endotracheal tube (ETT) and central lines.

Preparation:

- Preoxygenation, empty stomach, suction ETT/oral cavity
- Remove ECG leads and reattach to back
- Support and frequently reposition pressure points: face, shoulder, anterior pelvis

Duration

Each session of prone position ventilation should be at least 16 hours per day.Response criteria to prone positioning.

Response to prone positioning should be assessed with arterial blood gas analysis collected after 2 hours. Patients who have increase in the PaO_2/FiO_2 ratio of 20 mmHg or an increase in PaO_2 >10 mmHg compared with supine position are considered responsive.

When to stop prone positioning?

a. In PROSEVA, prone positioning was stopped when PaO_2/FiO_2 remained ≥ 150 mm Hg 4 hr after supinating (with PEEP ≤ 10 cm H_2O and FiO_2 ≤ 0.6) the patient from prone positioning. (Clinical improvement)

b. PaO_2/FIO_2 ratio deterioration by more than 20% relative to supine or the occurrence of a life-threatening complication during prone position. (Clinical deterioration) We need to consider continuing prone positioning until clear improvement in gas exchange, mechanics, and overall clinical course.

Clinical impact and outcome

a. In PROSEVA multicenter RCT with severe ARDS, 28-day mortality was significantly lower in the prone group (16.0% vs 32.8% in the supine group, p<0.001). Unadjusted 90-day mortality was 23.6% in the prone group versus 41.0% in the supine group (P<0.001), with a hazard ratio of 0.44 (95% CI, 0.29 to 0.67).

b. In meta-analysis of six trials (1016 participants), prone ventilation when used with lung protective ventilation strategies, mortality was significantly reduced with prone positioning (risk ratio 0.74, 95% confidence interval 0.59–0.95; I2 = 29%) compared with supine position.

In patients with COVID-19 ARDS, prone positioning was found as effective in improving respiratory physiology and survival as in patients with non-COVID ARDS and prone positioning should be an essential therapeutic option.

1.4.5 Troubleshooting

This section describes important causes of ventilator troubleshooting and subsequent management briefly.

Common scenarios of troubleshooting

1. Ventilator alarms

2. Desaturation
3. Hypotension
4. Patient-ventilator asynchrony
5. Dynamic Hyperinflation

I. Ventilator Alarms: Ventilator alarms are used to warn the changes in patient's status or problems with the machine. Alarms are safety measures and should never be disabled.

A. High airway pressure
B. Low airway pressure
C. High tidal volume
D. Low tidal volume
E. Apnea or low respiratory rate

Always treat your patient first and the ventilator second !

- Examine patient and measure vital signs
- Review the alarm and ventilator parameters
- Try to find out the cause of the alarm: patient or circuit or ventilator?

i. High pressure alarms

The causes of high-pressure alarms depend on PIP and plateau pressure.

Table 6: Causes of high-pressure alarms

High peak pressure/Low plateau pressure	High peak pressure/High plateau pressure
Mucus plug	ARDS
Bronchospasm	Pulmonary edema
ET tube block/kinking	Pneumothorax, pleural effusion
Tube biting	ET tube migration to a single bronchus

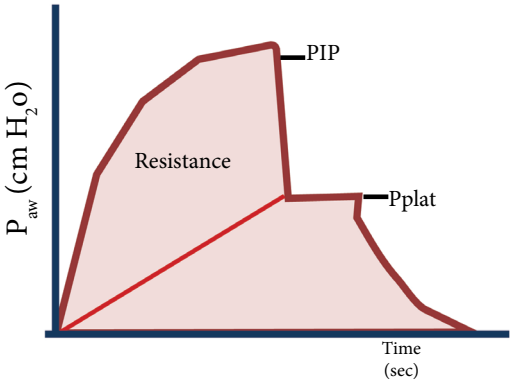


Figure 5 (A) High peak Pressure/Low Plateau Pressure

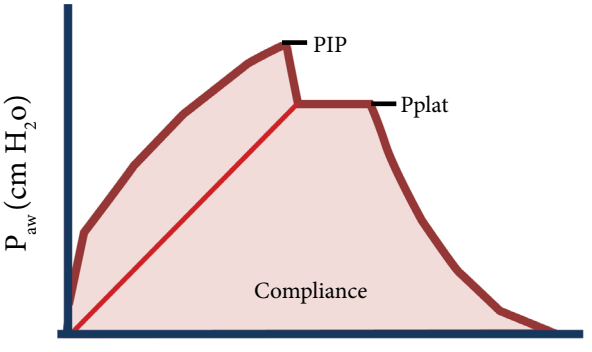


Figure 5 (B) High peak pressure/High Plateau Pressure

ii. Low pressure alarm

The following factors need to be looked for and managed if low pressure alarms ring.

1. Circuit factors

Circuit disconnection

- Loose circuit connection
- Leak from water trap
- Loose humidifier connection

2. ET tube factors

- Cuff leak (ET tube or Tracheostomy tube)
- ET tube pulled out

3. Patient factors

- Insufficient inspiratory flow
- Leak from chest tube

iii. Apnoea alarms

Ventilator does not sense a breath during set interval (20 seconds)

Causes

- Over sedation, or neurologic changes.
- No respiratory effort in spontaneous mode
- Inappropriate alarm settings
- Cardiopulmonary arrest.
- Rule out life threatening causes

Management

- Make sure Apnoea-Backup-Ventilation is ON
- Review settings
- Whenever in doubt manually ventilate the patient

II. Desaturation or hypoxemia: It refers to decrease in oxygen content of the blood commonly measured by pulse oximetry (SpO_2 <90%) or arterial blood gas analysis (PaO_2 < 60 mmHg). The immediate intervention must be increase FiO_2 to 1.0 and look for the cause(s).

a. Rule out major technical complications:

- Endobronchial intubation
- Accidental extubation
- Lobar/lung collapse
- Pneumothorax
- Ventilator malfunction

b. Assure ventilator synchrony: sedation, paralysis

c. Ventilator setting adjustment including PEEP (ARDS net table)

d. Prone positioning

Bed side ultrasonography or Chest X-ray may be required to find the cause.

III. Hypotension

Important causes of hypotension after the initiation of mechanical ventilation are:

- Relative hypovolaemia
- Drug induced vasodilation and myocardial depression
- Dynamic hyperinflation
- Tension pneumothorax

Management

- Hypotension due to relative hypovolaemia or anaesthetic induction agents usually responds rapidly to fluid.
- Hypotension due to gas trapping needs adjustment of ventilator settings (e.g., prolonging expiratory time, decreasing respiratory rate, etc.), and giving bronchodilators.

IV. Patient-Ventilator Asynchrony

Patient–ventilator asynchrony is most commonly recognized as a patient who seems to be "fighting" the ventilator, either inspiratory or expiratory phase is not in synchrony with the ventilator. It is a mismatch between the patient demand for flow, volume, or pressure and what the ventilator is supplying to the patient. Patient-Ventilator asynchrony occurs when the patient's demands are not met by the ventilator, resulting from problems with timing of inspiration, adequate inspiratory flow for demand, timing of the switch to expiration and duration of inspiration.

Causes:

1. Patient factors-ventilatory drive, ventilatory requirements, delirium

2. Ventilator factors- inspiratory trigger (flow, volume, or pressure), delivery mechanism (flow, volume, or pressure), cycling criteria (when ventilator stops assisting inspiration and allows passive exhalation)

Types of ventilator asynchrony

a. Ineffective triggering

b. Inappropriate triggering -patient inspires while the ventilator cycles to expiration

c. Auto-triggering

d. Flow asynchrony (too fast or too slow)

e. Exhalation asynchrony (too early or too late)

Assessment

i. Clinical Examination- respiratory pattern, audible sounds (e.g., cuff leak, stridor, wheeze), vital signs-$ETCO_2$, SpO_2, chest findings

ii. Ventilator- waveforms, alarms

Management

a. Address life threats hypotension, desaturation

b. Disconnect patient from ventilator and replace with BVM if required

c. Treat patient's respiratory pathology affecting resistance and/ or compliance (e.g., sputum, bronchospasm, chest wall eschar, pneumothorax)

d. Treat other patient factors (e.g., pain, sleep, sedation, delirium, nutrition)

e. Correct problems with the endotracheal tube (kinking, secretions)

f. Choose appropriate ventilator settings (mode, trigger, respiratory rate, flow)

V. Intrinsic PEEP and Dynamic Hyperinflation

Expiration is a passive process of exhaling air and resistance to air flow (e.g., bronchospasm) results in decreased expiratory flow which may lead to longer time to expire full tidal volume. Inspiration starts before end of expiration. Residual air remains in the chest exerting pressure in the respiratory circuit. It increases alveolar pressure at the end of expiration above zero (zero being the atmospheric pressure). This process of incomplete emptying is called dynamic hyper-inflation, and the positive alveolar pressure is called intrinsic PEEP or auto-PEEP.

Clinical features of dynamic hyperinflation

a. Prolonged expiratory phase (by auscultation)
b. Increased chest distension
c. Decreased chest expansion
d. Decreased breath sounds bilaterally
e. Auto-PEEP in the expiratory hold manoeuvre
f. Increased peak airway and plateau pressures
g. Increased plateau pressures

Causes of auto-PEEP

Increased resistance to expiratory flow could be due to machine factors, ventilator setting and patient factors.

A. Machine factors

i. Blocked or faulty expiratory valve of the ventilator
ii. Kinked expiratory limb of the ventilator tubing
iii. Rain-out in the expiratory limb
iv. Clogged water sodden HME
v. Kinked ET tube/tube bite
vi. ETT clogged with sputum

B. Ventilator settings

i. Short expiratory time eg; in very high respiratory rate
ii. High I: E ratio
iii. Increased respiratory rate

C. Patient factors

i. Bronchospasm

The auto-PEEP is measured by expiratory breath hold maneuver.

Effects of Auto-PEEP

The effects of auto PEEP are:

a. Reduce venous return which in turn can cause decreased cardiac output, diminished perfu-sion of respiratory muscles and respiratory fatigue.

b. Increases work of breathing, as the auto PEEP must be reversed before inspiratory airflow begins / ventilator is triggered. For example, when the auto-PEEP level is 5 cm H_2O and the sensitivity is set at -2 cm H_2O, the pressure gradient (DP) to trigger a mechanical breath becomes 7 cm H_2O.

c. Increased intra-thoracic pressure leading to decreased venous return and hemodynamic instability.

Measures to reduce auto-PEEP

i. Improving ventilation and reducing air trapping by bronchodilators and steroids

ii. Correcting machine factors, e.g., empty the water out of the tubes, change the HME, change the ventilator valve

iii. Suction ETT, ensure patency

iv. Prolonging the expiratory time by increasing the flow rate or reducing the tidal volume or frequency decreasing I: E ratio

v. Use of extrinsic PEEP (about 85% of auto-PEEP)

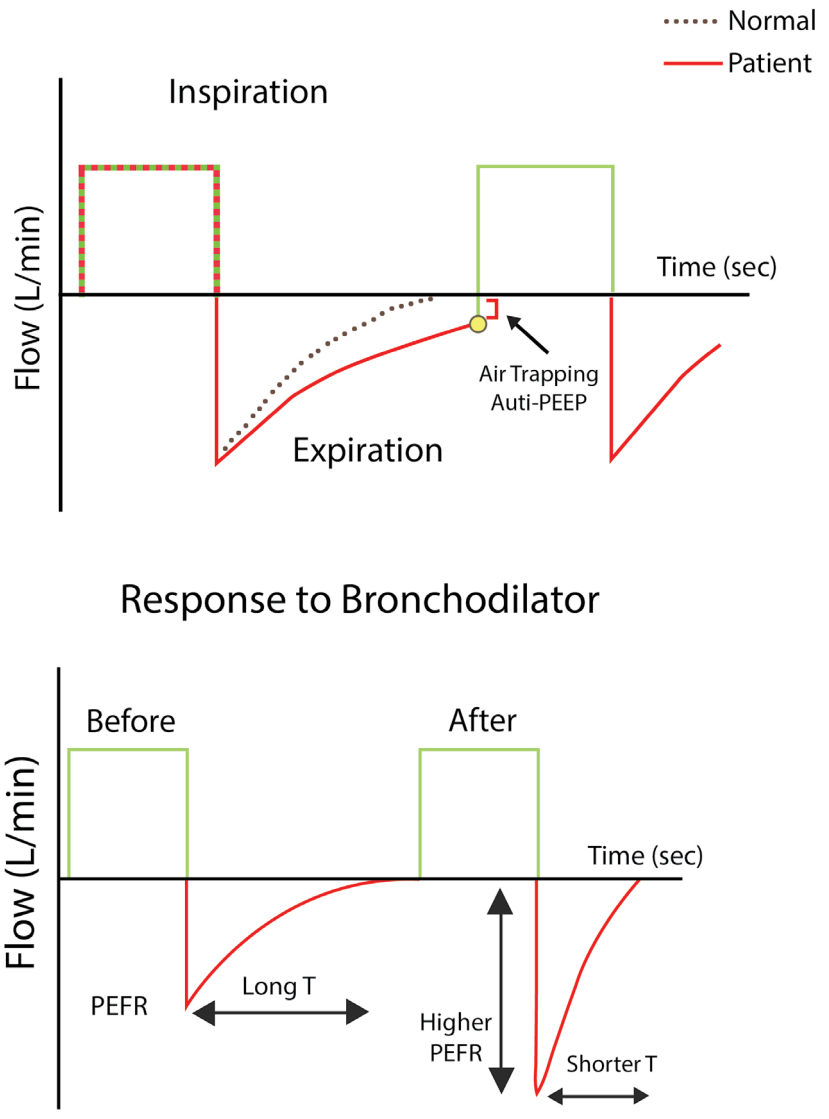


Figure 6: Auto-PEEP and Response to bronchodilator

1.4.6 Newer Modes

Airway Pressure Release Ventilation (APRV) and High Frequency Oscillation Ventilation.

I. Airway Pressure Release Ventilation (APRV)

It is a pressure-controlled mode of ventilation that delivers an almost continuous positive pressure with intermittent, time-cycled, short releases at a lower pressure. Spontaneous ventilation is encouraged, and the relatively increased mean airway pressures allow 'open-lung' ventilation.

Nomenclature: P-high, P-low, T-high, and T-low

P-high describes the highest level of pressure applied to the respiratory system, and T-high describes the time in seconds spent at this pressure. P-low is the lowest pressure applied by the ventilator to the respiratory system, and T-low indicates the time in seconds spent at this pressure. P-low is normally set at zero cmH_2O, but T-low is short and titrated, such that intrathoracic pressure never reaches atmospheric pressure.

Maintaining a prolonged high pressure (P-high) maximizes the recruitment of available lung tissue and therefore improves oxygenation, an example of the 'open-lung' approach to invasive ventilation. Short and relatively infrequent periods at a lower pressure (P-low) facilitate carbon dioxide clearance. While any patient can be adequately supported using APRV, it is generally used for patients who require recruitment of alveoli to maintain oxygenation, such as in ARDS (along with other treatments such as neuromuscular blockade, PEEP, and prone position). This mode has been used as rescue therapy in severe ARDS.

i. Initial APRV Settings

1. Set FiO_2 to 1.0 and can be reduced rapidly as required with target SpO_2 90% and FiO_2 <0.5.

2. P-high at the Pplateau (or desired Pmean + 3 cmH_2O). If mean airway pressure is known from previous mode, then P-high can be set at the previous mean airway pressure. A good starting level would be 28 cm H_2O and can be increased by 2 cm H_2O each time to improve oxygenation.

3. Set P-low to 0 cmH_2O.

4. Set T-high to 5 s (range: 3–8 s)

5. Set T-low initially to 0.5 s (range: 0.3–0.8 s). T-low should be short enough to terminate expiratory flow at approximately 75% of peak expiratory flow (PEFR). The expiratory time should be short enough to prevent de-recruitment and long enough to obtain a suitable tidal volume.

6. The respiratory rate should be 8 to 12 breaths per minute.

7. Automatic tube compensation (ATC) should be on if spontaneously breathing.

8. The use of shorter-acting sedative medications allows for easier titration.

ii. Monitoring a patient on APRV

APRV mode uses the diaphragm and provide rest to other inspiratory muscles. Anterior chest muscles will move less. The patient should be breathing more comfortably as recruitment occurs.

The alveolar recruitment will be better if started earlier in ARDS. When ARDS patients are not comfortable despite optimal APRV settings, an alternative mode should be used.

II. High Frequency Oscillation Ventilation (HFOV)

High-frequency oscillatory ventilation (HFOV) is a rescue maneuver to maintain lung recruitment, avoid overdistention for failed conventional mechanical ventilation. It does not rely on bulk flow for oxygenation and ventilation. Small tidal volume (1-4mL/kg) is delivered at high frequencies (3-15 Hz) with an oscillatory pump to maintain constant lung recruitment aiming to prevent lung injury from overdistention and loss of recruitment (atelectrauma). HFOV maintains alveolar inflation at a near constant airway pressure with a sinusoidal flow oscillation to prevent the lung "inflate–deflate" cycle and provides improved oxygenation with reduced incidence of barotrauma. Patients receiving HFOV require a greater amount of sedation and neuromuscular blockade.

ARDS is a heterogeneous lung disease with different phenotypes, there may be some patient subgroups that might be helped (e.g., patients with homogeneous, recruitable lung) while others are harmed. HFOV found to cause harm or have no benefit in the recent RCTs in adult ARDS patients.

HFOV should not be a routine part of the management of ARDS patients. Common contraindications are ET tube displacement, airway obstruction by mucus plugging, pneumothorax, bronchospasm, multiple organ failure etc. There is no evidence supporting APRV or HFOV in relation to mortality and morbidity.

1.4.7 Liberation from Mechanical Ventilation

Mechanical ventilation is a life-saving intervention and patients should be liberated from the ventilator as soon as the underlying condition that led to mechanical ventilation has improved sufficiently and the patient is able to safely maintain spontaneous breathing. It is three-step procedure: readiness testing, weaning and extubation. This section briefly describes the process of liberation from mechanical ventilation.

I. Readiness Testing

Objective criteria with some physiological tests are used to decide whether patient is ready to begin weaning. Two protocolized paired spontaneous awakening trials (SATs) and spontaneous breathing trials (SBTs) are used to assess safety individually. SBT is only performed once the patient passes the safety screen for SAT.

Use of protocol-based criteria helps to reduce the duration and risks of mechanical ventilation and prevents premature weaning (Risks summarized in Table 7).

SAT safety screen

a. No active seizures

b. No alcohol withdrawal

c. No agitation

d. No paralytics

e. No myocardial ischemia

f. Normal intracranial pressure

SAT failure

a. Anxiety, agitation, or pain

b. RR >35 breaths/minute

c. SpO_2< 88%

d. Respiratory distress

e. Acute cardiac arrhythmias

Use of protocol-based criteria helps to reduce the duration and risks of mechanical ventilation and prevents premature weaning.

Table 7: Risks of mechanical ventilation:

Risks with prolonged ventilation	Risks with premature liberation
Volutrauma, Barotrauma, VALI	Loss of airway protection
Airway injuries, ET tube complications	Hypoxemia, risk o f cerebral hypoxia
Prolonged sedation, neuromuscular weakness	Cardiovascular stress
Ventilator associated pneumonia	Muscle fatigue
Pressure sores	Reintubation & further Airway injuries

Table 8: Checklist for identifying candidates for a trial of spontaneous breathing trial (SBT)

Respiratory criteria • $PaO_2/FiO_2 \geq 150\text{-}200$ mmHg with $FiO_2 \leq 0.50$ and PEEP ≤ 8 cmH_2O • $PaCO_2$ normal or baseline levels • Patient able to initiate inspiratory effort
Cardiovascular criteria • No evidence of myocardial ischemia • Heart rate ≤ 140 beats/minute • Blood pressure adequate with no or minimal vasopressors
Mental status* • Arousable patient or GCS ≥ 13
Absence of correctable co-morbid conditions • No fever • No significant electrolytes abnormalities

**Spontaneous awakening trials (SATs)*

Table 9: Respiratory parameters used to predict a successful trial of spontaneous breathing

Measurement*	Threshold for success	Range of likelihood ratio
Tidal volume (Vt)	4-6 ml/kg	0.7-3.8
Respiratory rate (RR)	< 35 bpm	1.0-3.8
RR/Vt (Rapid shallow breathing index, RSBI)	60-105bpm/L	0.8-4.7
Maximum inspiratory pressure (MIP)	-15 to -30 cm H2O	1.0-3.0

**All parameters should be measured after at least 2 minutes of SBT.*

SBT conducted while the patients breathe through ventilator circuit with low pressure support (5 cm H_2O to overcome resistance of circuit) has the advantage of monitoring respiratory parameters: tidal volume, respiratory rate and RSBI. The disadvantage is increased work of breathing.

Contraindications for Liberation

- Serious/life threatening cardiac arrhythmia
- Active myocardial ischemia
- Very high metabolic rate (MV > 12L/min)
- Chest wall instability

Some patients deemed ready to wean may fail a subsequent spontaneous breathing trial (SBT). Though failed weaning has not been shown to be harmful, patient needs close monitoring. Ventilatory support should be started at the first sign of intolerance (i.e., ventilatory fatigue should be avoided). In suchcases, cause(s) of liberation (weaning) failure (given in table 11) should be investigated and treated.

Table 10: Clinical criteria and threshold for SBT failure

• General: agitation or distress, depressed mental status, diaphoresis & evidence of increasing effort
• SpO_2< 90% on FiO_2 ≥ 0.50
• PaO_2 ≤ 60 mmHg on FiO_2 ≥ 0.50
• $PaCO_2$ >50 mmHg or increase by 8 mmHg from baseline of SBT
• pH <7.32 or decrease by 0.007 from baseline of SBT
• RSBI > 105 bpm/L
• RR >35 bpm or increase by ≥ 50% from baseline of SBT or < 8 breaths per minute
• HR > 140 bpm or increase by ≥ 20% from baseline of SBT
• Systolic BP>180 mmHg or increase by ≥ 20% from baseline of SBT
• Systolic BP < 90 mmHg
• Cardiac arrhythmias

Table 11: Causes of Liberation Failure

• Critical illness neuropathy
• Electrolyte disturbances: Hypophosphatemia, Hypokalemia, Hypomagnesemia, Hypocalcemia (ionized)
• Malnutrition
• Myocardial ischemia
• pH <7.32 or decrease by 0.007 from baseline of SBT
• Fluid overload
• Adrenal insufficiency

II. Weaning

Weaning is the process of decreasing the degree of ventilator support and allowing the patient to assume a greater proportion of their own ventilation (e.g., spontaneous breathing trials or a gradual reduction in ventilator support.

Liberation from mechanical ventilator can be broadly divided into 4 types:

a. Simple Liberation: patient tolerates first SBT & is successfully extubated (~ 69% of all patients).

b. Difficult Liberation: Patient fails to tolerate initial SBT, successful weaning requiring up to 3 SBTs or within 7 days from first SBT. (31 % enter but only 16 % success within 7 day)

c. Prolonged liberation: Patient fails at least 3 SBTs or takes > 7 days after the first SBT. (~15 % of all patients)

d. Long-term Ventilator dependency: Less than 1 %

Liberation modes of ventilator

1. CPAP/PSV
2. T-piece with oxygen support
3. SIMV (least preferred)

When a patient successfully passes a SBTs, they should be evaluated for safety of extubation. This requires an assessment of the volume of respiratory secretions as well as airway patency and protection (i.e., has a sufficient cough and adequate level of consciousness)

III. Extubation

Extubation is the removal of the endotracheal tube (ETT) and is the final step in liberation from mechanical ventilation support.

Extubation should be performed when

a. The patient's medical condition is stable,

b. SBT has been successful,

c. The airway is patent, and ability of patient's cough strength and secretion clearance.

d. Any potential difficulties in reintubation have been identified.

Most patients should be extubated during daytime hours.

Assess risk for post-extubation stridor

Post-extubation stridor occurs in about 10% of critically ill patients and associated with increased rates of reintubation, prolonged duration of mechanical ventilation and longer length of ICU stay. Risks should be assessed prior to extubation through cough leak test though the reported sensitivity is 15- 85% and specificity 70-99%.

Common risk factors for post-extubation stridor

a. Prolonged intubation

b. Age ≥ 80 years

c. A large endotracheal tube (>8 mm in men, >7 mm in female)

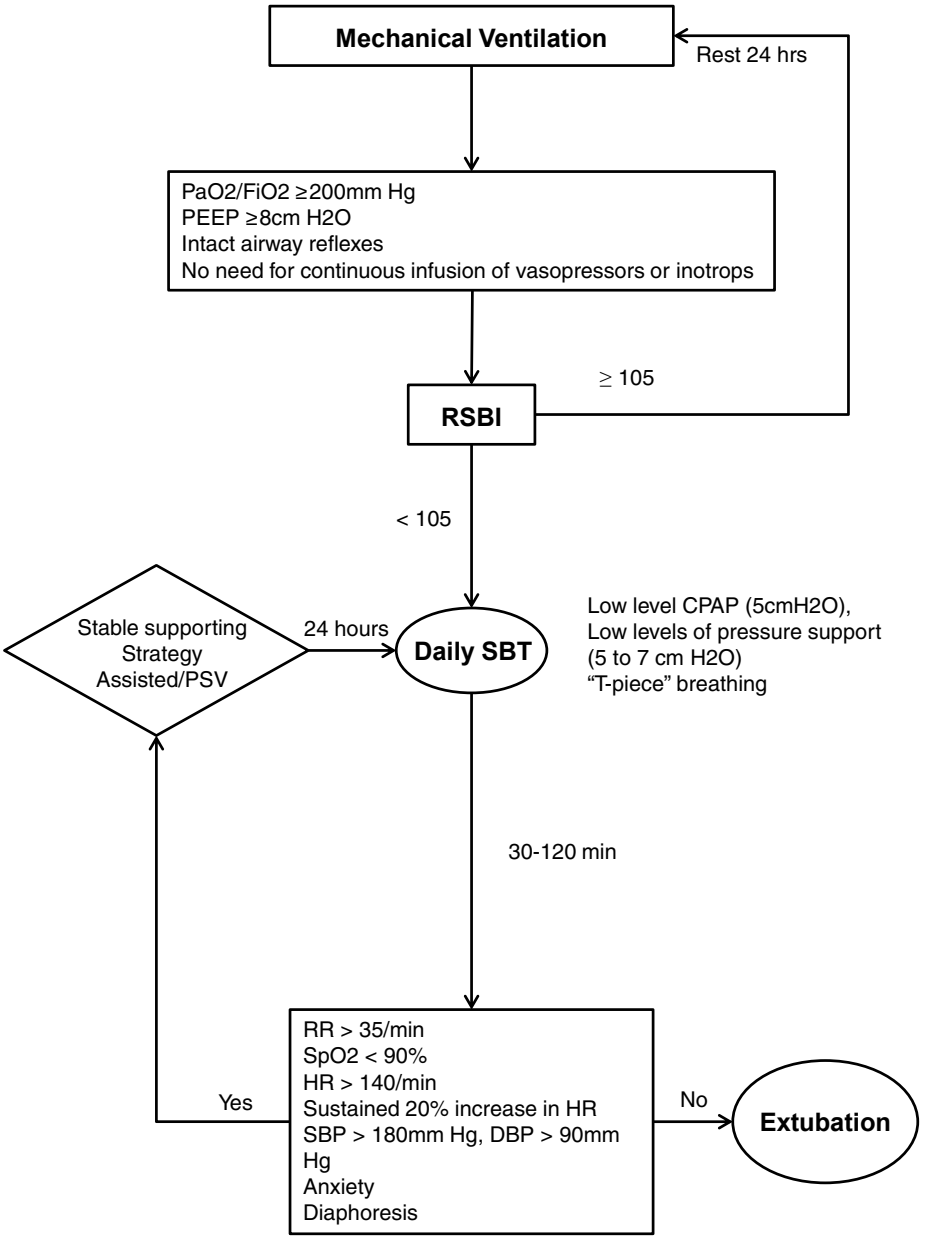
d. Traumatic intubation

e. Insufficient sedation

Cough leak test

a. Qualitative assessment is performed by deflating the cuff and then listening for air movement around the ETT by putting a stethoscope over the upper trachea. Absence of air movement may indicate laryngeal obstruction.

b. Quantitative assessment is performed by measuring the difference between the inspired and expired tidal volumes of ventilator-delivered breaths (VTi-VTe= cough leak volume) during volume-cycled mechanical ventilation after deflating the ETT cuff. The lowest three expired tidal volumes obtained over six breaths are averaged and then subtracted from the inspired tidal volume to give the cuff leak volume. If cough leak volume is <110 ml or < 12-24% of delivered tidal volume, it may suggest diminished airway patency and risk for post-extubation stridor whereas more than that is considered a normal cuff leak test. The usual practice is to proceed with extubation in patients with a sufficient cuff leak volume. In patients with an absent or reduced cuff leak, glucocorticoids should be given for at least 6-8 hours and reassessed with another cuff leak test and/or extubation.



Flowchart 2: Algorithm for Daily SBT and Extubation

1.4.8 Non-invasive Positive Pressure Ventilation (NIPPV)

Considerations:

- Take proper infection control precautions as it is a potentially aerosol generating. However, negative airflow room is not mandatory.

- Ensure masks/devices fit well and there is minimal air leak.

Figure 7: Non-invasive Positive Pressure Ventilation (NIPPV)

Non-invasive ventilation and HFNC have been suggested as an option even in well-established ARDS. In the patient with early ARDS with acute hypoxemic respiratory failure, HFNC has reduced mortality. However, there is lack of large-scale trial to suggest the optimal timing of intubation in ARDS. Mild cases of ARDS may be responded to noninvasive ventilation but most cases need intubation and ventilation along with sedation while underlying injury is treated.

2. Rescue Therapy

Extracorporeal Membrane Oxygenation (ECMO) Therapy

ECMO or Extra Corporeal Membrane Oxygenation is a form of extracorporeal life support where an external artificial circulation carries venous blood from the patient to a gas exchange device (oxygenator) where blood becomes enriched with oxygen and has carbon dioxide removed. This blood then re-enters the patient circulation.

Patients who are hypoxemic despite maximal conventional ventilatory support, who have significant ventilator-induced lung injury or who are in reversible cardiogenic shock may be considered for ECMO support. For respiratory failure, the basic premise is that ECMO will allow the level of ventilatory support to be reduced, which may allow time for recovery from the underlying pathology and recovery from ventilator-induced lung injury to occur.

The type of ECMO performed will depend on the patient's underlying cardiac function. Veno-venous (V-V) ECMO is usually performed for isolated respiratory failure, whereas Veno-arterial (V-A) ECMO (full cardiopulmonary bypass) is performed for combined cardiac and respiratory failure.

The term extracorporeal membrane oxygenation (ECMO) was initially used to describe long-term extracorporeal support that focused on the function of oxygenation. Subsequently, in some patients, the emphasis shifted to carbon dioxide removal, and the term extracorporeal carbon dioxide removal was coined.

Extracorporeal support was later used for postoperative support in patients following cardiac surgery. Other variations of its capabilities have been tested and used over the last few years, making it an important tool in the armamentarium of life and organ support measures for clinicians. With all of these uses for extracorporeal circuitry, a new term, extracorporeal life support (ECLS), has come into vogue to describe this technology.

Veno-venous ECMO

Veno-venous ECMO (VV ECMO) involves venous blood from the patient being accessed from the large central veins (via the "access line") and returned to the venous system near the right atrium (via the "return line") after it has passed through an oxygenator. It provides support for severe respiratory failure when no major cardiac dysfunction exists. When flow through a single access cannula is insufficient to support the high ECMO flow rate that may be required in severe respiratory failure, a second venous access cannula may be required.

VV ECMO improves the patient's oxygenation by reducing the amount of blood that passes through the lung without being oxygenated and in addition, removes CO_2 from the patient's blood. This allows the level of ventilatory support to be reduced which reduces ventilator-induced lung injury.

The efficiency of oxygenation by the ECMO circuit depends on the pump flow relative to the patient's cardiac output. The patient's oxygenation should increase with increasing ECMO flow rate, if this does not occur, recirculation of blood between the inflow and outflow cannula should be suspected.

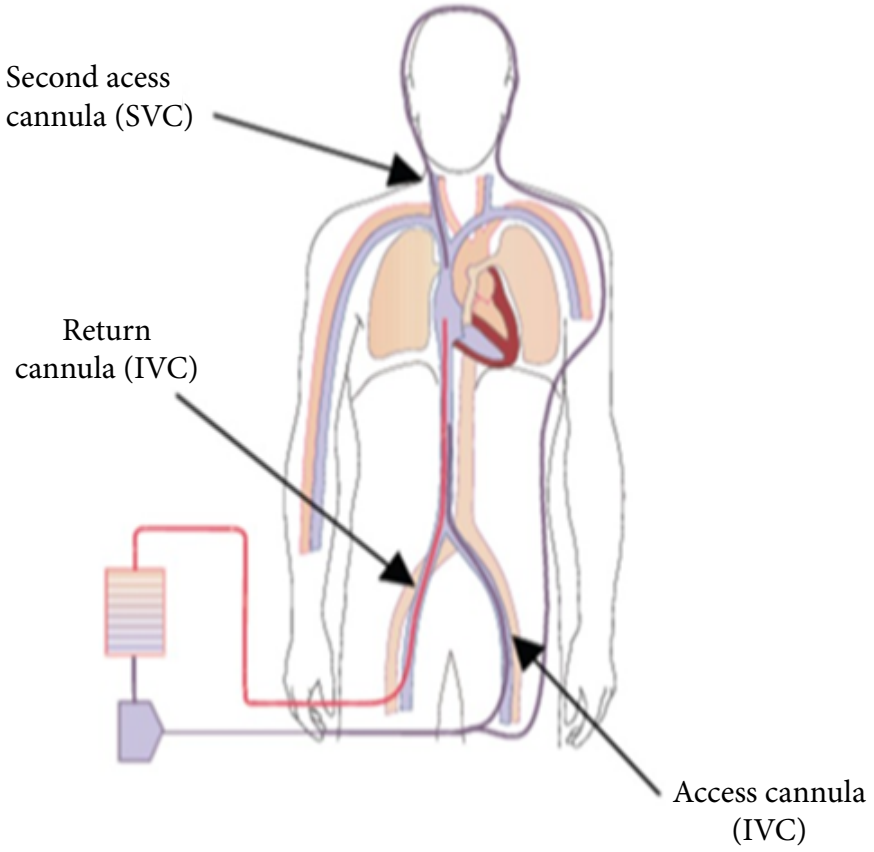


Figure 8: Venous –venous ECMO Circuit

V-V ECMO is more efficient at removing CO_2 from the blood than delivering oxygen. The amount of CO_2 removal depends on the ECMO flow rate relative to the patient's cardiac output and depends on the oxygen flow rate to the oxygenator. Increasing oxygen flow rate decreases the CO_2 in the blood leaving the oxygenator (analogous to the effect that increasing minute ventilation has on arterial PCO_2). The oxygen flow rate to the oxygenator should be roughly twice the ECMO flow rate. With an ECMO flow rate of approximately 2/3rd the patient's cardiac output, and oxygen flow rate of twice the pump flow, the oxygenator can remove nearly all the patient's CO_2 production.

Veno-arterial ECMO

Veno-arterial ECMO (VA ECMO) involves venous blood from the patient being accessed from the large central veins and returned to a major artery after it has passed through the oxygenator. It provides support for severe cardiac failure, (usually with associated respiratory failure), most commonly after cardiac surgery.

Low flow veno-arterial ECMO is a transitory form of ECMO support in which small cannulae (quicker to insert) are inserted percutaneously. It is an emergent resuscitative intervention (also known as ECMO-CPR).

VV ECMO or VA ECMO?

When considering indications of one form over other, the following advantages and disadvantages must be considered.

V-V ECMO avoids the risks of potentially serious arterial injury and the consequences of air or clot embolization from the circuit are less severe.

V-V ECMO is a low-pressure circuit compared to veno-arterial, resulting in less stress on the circuit tubing and the oxygenator and may thereby improve their longevity. V-V ECMO produces less hemodynamic disturbance than veno-arterial as blood is withdrawn from and returned to the same side of the circulation. For example, increasing V-V ECMO flow will not cause any change in the CVP, whereas increasing V-A ECMO flow will reduce the CVP (pulmonary blood flow). Finally, there is animal tested evidence that the preservation of pulmonary blood flow that occurs with V-V ECMO promotes more rapid recovery from pulmonary sepsis than does V-A ECMO.

The major advantage of V-A over V-V ECMO is that it provides complete hemodynamic and respiratory support. It may be indicated for severe cardiac failure following cardiac surgery either as a bridge to recovery or to another destination therapy (heart transplant or to another implantable support device). Other indications for V-A ECMO in an adult are cardiogenic shock associated with myocarditis, poisoning or hypothermia.

Indications of ECMO

A. In hypoxic respiratory failure due to any cause (primary or secondary) ECLS should be considered when the risk of mortality is 50% or greater and is indicated when the risk of mortality is 80% or greater.

- 50% mortality risk is associated with a PaO_2/FiO_2 < 150 on FiO_2 > 90% and/or Murray score 2- 3, AOI score 60, or APSS score
- 80% mortality risk is associated with a PaO_2/FiO_2 < 100 on FiO_2> 90% and/or Murray score 3-4, AOI >80, APSS 8 despite optimal care for 6 hours or less
- The best outcome in ECMO for adult respiratory failure occurs when ECMO is instituted early after onset (1-2 days)

B. CO_2 retention on mechanical ventilation despite high Pplat (>30 cm H2O)

C. Severe air leak syndromes

D. Need for intubation in a patient on lung transplant list

E. Immediate cardiac or respiratory collapse (PE, blocked airway, unresponsive to optimal care)

Contraindications to ECMO

There are no absolute contraindications to ECLS, as each patient is considered individually with respect to risks and benefits. There are conditions, however, that are associated with a poor outcome despite ECLS, and can be considered relative contraindications.

A. Mechanical ventilation at high settings (FiO_2 >.9, P-plat >30) for 7 days or more. Many centers do not consider time on ventilation a contraindication.

B. Major pharmacologic immunosuppression (absolute neutrophil count <400 mm3)

C. CNS hemorrhage that is recent or expanding

D. Non-recoverable comorbidity such as major CNS damage or terminal malignancy

E. Age: no specific age contraindication but consider increasing risk with increasing age

3. Pharmacological Therapy

3.1 Role of Corticosteroids in ARDS

The role of systemic corticosteroids for treatment of ARDS is much debated. The theoretical benefits of reduced lung inflammation and fibrosis must always be weighed against the harms such as hyperglycemia, nosocomial infections, ICU acquired weakness and delirium. Studies conducted before the lung protective ventilation era did not show mortality benefit with systemic steroids in ARDS. A few newer studies and meta-analysis have shown beneficial effect of early (before 14 days) use of steroids in ARDS in terms of reduced Ventilator-free and ICU-free days and decreased in-hospital mortality. The doses used in these trials were: Methylprednisolone 1-2 mg/kg/day; Dexamethasone 20 mg/day from D1-D5 and 10 mg/day from D6-D10. On the contrary, use of corticosteroids for H1N1 ARDS is associated with increased mortality. Since there is a lot of heterogeneity in terms of dose, timing and agent used leading to low certainty evidence, currently a state of equipoise exists regarding recommendations for systemic steroid use in ARDS.

i. Intravenous Hydrocortisone 200 mg IV/Day in continuous infusion or in four divided doses should be used in ARDS patients with septic shock

ii. Dexamethasone 6 mg/day IV or equivalent dose of steroids should be used in COVID ARDS for total duration of 10 days or for as long as the patient requires oxygen

iii. Corticosteroid should not be used in ARDS due to H1N1 influenza or other etiologies

3.2 Others Pharmacologic Therapy

Inhaled Nitric Oxide (iNO) induces pulmonary artery vasodilation and improve gas exchange by reducing the intrapulmonary shunt. Small studies have demonstrated benefit in patients with refractory hypoxemia not improving despite lung protective ventilation and prone positioning.

However, many studies have failed to demonstrate benefit in outcomes of ARDS patients, and the therapy is expensive. Trials of multiple other drugs like high dose Vitamin D, high dose Vitamin C, prostaglandin E1, statins and Interferon-B-1a have failed to demonstrate consistent benefit in ARDS. These pharmacological agents should be considered investigational, and we do not recommend their routine use in patients with ARDS.

4. Fluid management in ARDS

ARDS is characterized by increased permeability of alveolar-capillary bed; hence an increased hydrostatic pressure in the pulmonary vasculature caused by intravenous fluid may lead to alveolar flooding and worsening hypoxemia. On the other hand, when multiorgan dysfunction occurs in the setting of ARDS, intravenous fluids may be essential to maintain adequate tissue perfusion. In patients with ARDS who do not require vasopressor support, a fluid conservative strategy increases the number of ventilator free days as compared to liberal fluid strategy without increasing the risk of acute kidney injury or need for dialysis. Hence, a net even or a slight negative balance of 500 ml – 1000 ml may be targeted by avoidance of excess intravenous fluid infusion or sometimes by use of diuretics or hypertonic albumin in patients who are not in shock.

Traditionally, targeting a central venous pressure < 4 mm Hg or Pulmonary Artery Occlusion Pressure < 8 mm Hg have been used to determine intravenous fluid administration. More recently, fluid responsiveness in critically ill patients is assessed by dynamic measures like pulse pressure variation, passive leg raises, end-expiratory occlusion, rapid or mini fluid challenge. Extravascular Lung Water Index (EVLWI) and Pulmonary Vascular Permeability Index (PVPI) as measured by transpulmonary thermodilution, may help to prevent excessive volume expansion during initial resuscitation as well as prompt initiation of fluid removal during the post resuscitation phase.

i. Fluid restriction strategy should be the norm in patients with ARDS.

ii. Negative fluid balance of 500 ml- 1000 ml should be targeted by avoiding excess intravenous fluid infusion or sometimes using diuretics/hypertonic albumin in patients who are not in shock.

5. Routine care of Critically Ill Patient

5.1 Protocolized Bundles in ICU

5.1.1 VAP Bundle: Ventilator Associated Pneumonia Prevention Bundle

1. Elevate the Head of the Bed to 30-45°

2. Perform continuous aspiration of sub-glottic secretion and/or suctioning of the ET tube periodically.

3. Ensure the ET tube cuff pressure is between 20-30 cm H_2O

4. Use Orogastric tube for feeding patients in mechanical ventilation. DO NOT USE nasogastric tube for feeding, continuous temperature monitoring in mechanically ventilated intubated/tracheostomized patients.

5. Use closed suction system for suctioning of endo-tracheal tube in all intubated/tracheostomized patients. DO NOT USE open suctioning system for endotracheal/tracheostomy suction.

6. Apply Oral Chlorhexidine solution to the oral cavity at least every 4 hours.

7. Interrupt the sedative drugs daily from in the morning and perform a standardized weaning protocol such as Spontaneous Breathing Trial (SBT) daily in the morning.

8. Use stress ulcer prophylaxis (SUP) in the form of intravenous/oral Ranitidine. Do NOT use PPI for prophylaxis of SUP in ICU.

9. Use DVT Prophylaxis in form of Subcutaneous Heparin. If contraindicated, use Sequential compression device (SCD) pumps.

5.1.2 Central Line Bundle: Prevention of Catheter-Related Blood Stream Infections (CRBSI)/Central Line Associated Blood Stream Infections (CLI)

During Central Line Insertion

- Scrub hands (Surgical hand wash) with iodine-based solution / soap.
- Use maximal sterile barrier (MSB) precautions, including the use of a cap, mask, sterile gown, sterile gloves, and a sterile full body drape, for the insertion of CVCs, PICCs, Dialysis Catheters, or even only catheter/guide wire exchange.
- Prepare clean skin with a 2 % Chlorhexidine preparation before central venous catheter and peripheral arterial catheter insertion and during dressing changes. If there is a contraindication to Chlorhexidine, then tincture of iodine, an iodophor, or 70% alcohol can be used as alternatives.
- Secure with silk sutures both at the length indicator of the catheter AND at the body of the catheter.
- Cover the full length of the catheter including the body with the dressing.
- Use either sterile gauze or sterile, transparent, semipermeable dressing to cover the catheter site.

Note:

Maximum sterile barrier (MSB) precautions are defined as wearing a sterile gown, sterile gloves, and cap and using a full body drape (similar to the drapes used in the operating room) during the placement of CV.

Maintenance of Central Line / Central Line Care

- Promptly remove any intravascular catheter that is no longer essential.
- Use Chlorhexidine solution 2% for catheter site dressing.
- If the patient is sweating or if the site is bleeding or oozing, use gauze dressing until this is resolved.
- Replace catheter site dressing if the dressing becomes damp, loosened, or visibly soiled.
- Wear either clean or sterile gloves when changing the dressing on intravascular catheters.
- Do not use topical antibiotic ointment or creams on insertion sites, except for dialysis catheters, because of their potential to promote fungal infections and antimicrobial resistance.
- Replace dressings used on short-term CVC sites every 2 days for gauze dressings.
- Replace dressings used on short-term CVC sites at least every 7 days for transparent dressings.
- Evaluate the catheter insertion site daily by palpation through the dressing and by inspection if a transparent dressing is in use.
- In patients not receiving blood, blood products or fat emulsions, replace administration sets that are continuously used no more frequently than at 96-hour intervals, but at least every 7 days.

• Replace tubing used to administer blood, blood products, or TPN within 24 hours of initiating the infusion.

5.1.3 ABCDE Bundle: Awakening and Breathing and Breathing Coordination, Delirium Monitoring /Management and Early Mobility (ABCDE) Bundle

• Every mechanically ventilated patient receiving a sedative will receive both a spontaneous awakening trial (SAT) and a spontaneous breathing trial (SBT) daily.

• ICU Nurse will perform the Spontaneous Awakening Trial (SAT).

• ICU Resident will perform the Spontaneous Breathing Trial (SBT).

Four Major Steps in The Awakening and Breathing Trial Coordination Process

Step 1. SAT Safety Screen: ICU Nurse

• The nurse should determine if it is safe to interrupt sedation by responding to the following questions:

- Is patient receiving a sedative infusion for active seizures?
- Is patient receiving a sedative infusion for alcohol withdrawal?
- Is patient receiving a paralytic agent (neuromuscular blockade)?
- Is patient's Richmond Agitation and Sedation (RASS) score >2?
- Is there documentation of myocardial ischemia in the past 24 hours?
- Is patient's intracranial pressure (ICP) high?
- Is patient receiving sedative medications to control intracranial pressure?

• If any of the above questions are answered **YES,** the nurse should conclude that it is **NOT SAFE** to stop patient's analgesic or sedative drugs. The nurse should continue the patient's regimen and reassess in 24 hours.

• The interdisciplinary team should then discuss the patient's condition during rounds and plan further.

Step 2. Spontaneous Awakening Trial (SAT): ICU Nurse

• If the patient passes the SAT Safety Screen, the nurse should hold all analgesic and sedative boluses from 6 AM.

• The nurse should determine if the patient tolerated interruption of sedation by assessing if the patient demonstrates any of the following SAT failure criteria:

- RASS score > 2 for 5 minutes or longer
- Pulse oximetry reading of < 88 % for 5 minutes or longer
- Respirations >35 breaths per minute for 5 minutes or longer
- New Acute Cardiac Arrhythmia
- Two or more of the following symptoms of respiratory distress
  - Heart rate increases by 20 or more beats per minute
  - Heart rate is less than 50 beats per minute

- Use of accessory muscles is observed
- Abdominal paradox
- Diaphoresis
- Dyspnea

• If the patient displays any of the above symptoms, the nurse should conclude the patient has failed the SAT.

• The nurse should restart the patient's sedation at 1⁄2 the previous dose, and then titrate to sedation target.

• If the patient can open his/her eyes to verbal stimulation without failure criteria (regardless of trial length) or does not display any of the failure criteria after 4 hours of shutting off sedation, the nurse should conclude the patient has passed the SAT.

• The nurse should then ask the ICU Doctor to perform a SBT safety screen.

Step 3. SBT Safety Screen: ICU Doctor (Fellow/Resident/Medical Officer)

• The ICU Doctor should determine if is safe to perform a SBT by responding to the following questions:

- Is the patient a chronic/ventilator dependent patient?
- Is the patient's pulse oximetry reading <88%?
- Is the patient's fraction of inspired oxygen (FiO_2) >50%?
- Is the patient's set positive end expiratory pressure (PEEP) >7?
- Is there documentation of the patient having myocardial ischemia in the past 24 hours?
- Is the patient's ICP high?
- Is the patient receiving mechanical ventilation to control ICP?
- Is the patient currently on high-dose vasopressor medications?
- Does the patient lack inspiratory effort?

• If any of the above questions are answered YES, the ICU Doctor should conclude that it is not safe to perform SBT and the ICU Doctor should continue mechanical ventilation and repeat SBT Safety screen again after 12 hours or in 24 hours.

• The ICU Doctor should ask the nurse to restart sedatives at half the previous dose only if needed.

• The interdisciplinary team should discuss the patient's condition during round and plan further.

Step 4. Spontaneous Breathing Trial (SBT): ICU Doctor

• If the patient passes the SBT Safety Screen, the ICU Doctor should perform SBT

• The Resident should determine if the patient tolerated the spontaneous breathing trial by assessing if the patient demonstrates any of the following spontaneous breathing trial failure criteria:

- Respiratory rate >35 breaths per minute for 5 minutes or longer
- Respiratory rate <8 Pulse oximetry reading of <88%
- Two or more of the following symptoms of respiratory distress
  - Use of accessory muscles

- Abdominal paradox
- Diaphoresis
- Dyspnea
- Mental status changes
- Acute cardiac arrhythmia

• If the patient displays any of the above symptoms, the ICU Doctor should conclude the patient has failed the SBT. The ICU Doctor should restart mechanical ventilation at previous settings.

• If the patient tolerates spontaneous breathing for >120 minutes without failure criteria, the ICU Doctor should inform the nurse and ICU Consultant that the patient has passed SBT and proceed for extubation (if other criteria meet) or as planned.

5.2 Protocol for Use of Sedatives and Analgesics in ICU

• Every patient admitted to an adult ICU should undergo routine sedation and delirium assessment using standardized, validated assessment tools.

• A nurse should perform and record the results of the Richmond Agitation and Sedation Scale (RASS) every 2 hours with Vital Signs. See Appendix for RASS Score.

• A Nurse should perform and record the results of the Confusion Assessment Method-ICU (CAM- ICU) twice a day or Intensive Care Delirium Screening Checklist (ICDSC) and whenever a patient experiences a change in mental status. See Appendix for CAM ICU and ICDSC.

• Each day during rounds, the team should set "target" RASS score for the patient to be maintained for the following 24 hours.

• Each day during interdisciplinary rounds, the Nurse should inform the team of the:
- Patient's "Target" RASS score
- Patient's actual RASS score
- Patients CAM-ICU status or ICDSC Score
- Sedative and analgesic medications the patient is currently receiving

5.2.1 Drugs Used for Sedation and Analgesia in ICU:

i. Propofol:

• Dose: 25-50 mcg/kg/min and titrate in increments of 25mcg/kg/min till desired level of sedation is achieved

• More appropriate for targeting deep sedation (RASS = - 2 / -3)

• Check Triglycerides after 72 hours

• Watch for lactic acidosis and rhabdomyolysis

• Should be used in increment of 5 ml/hour

• DOES NOT have Analgesic Property and so consideration to add analgesics into the patient's drug regimen

• Respiratory/Airway support may be needed, so preferred only in intubated/tracheostomy patients and requires close respiratory monitoring

ii. Fentanyl:

- Dose: 50-100mcg IV bolus
- Reassess in 15 minutes
- If inadequate pain relief, re-bolus fentanyl 50-100 mcg
- Re-evaluate again in 30 minutes and increase or decrease dose by 50% if inadequate or over-sedation
- If possible, avoid continuous infusion in ICU if planning for weaning / extubation from mechanical ventilation. Continuous Infusion is preferred only for very sick patients with refractory hypoxia, hemodynamically unstable who cannot be weaned and for acute pain management in post-operative surgical patients in ICU
- Fentanyl is used for sedation as intermittent bolus in patients planning to be weaned and extubated in near future.

iii. Morphine:

- Dose: 2- 5 mg IV then either 1-5 mg q 1 hr. prn or continuous infusion at 1-5 mg/hr. Reassess after 30 minutes, if inadequate pain relief, re-bolus Morphine 1-5 mg and increase drip by 50%. Re-evaluate again in 30 minutes and increase or decrease dose by 50 % if inadequate or over sedation.
- Very good sedative and analgesic property.
- Continuous Infusion preferred in sick patients with refractory hypoxia, hemodynamically unstable and are not planned for immediate weaning / extubation.
- If planned for immediate weaning/extubation, switch to intermittent bolus or other short acting drugs e.g., Fentanyl.

iv. Midazolam:

- Benzodiazepines MUST NOT be used for ICU Sedation.
- Used only for Anticonvulsant, and for Procedural Sedation, or Amnesia.
- Dose: 2 mg IV bolus followed by 1-2 mg q 1 hr. as needed titrated in increments of 1-2 mg IV after reassessing every 30 minutes till desired level is achieved.

v. Dexmedetomidine

- Bolus Dose: 0.5 mcg / Kg to 1 mcg / Kg IV
- Maintenance: Continuous infusion at 0.2 – 1 mcg / Kg / hour
- Side Effect: Bradycardia, Hypotension
- STOP If HR<60/min OR MAP<70mmHg
- Used for Procedural Sedation, Awake Intubation, Extubation, Agitation when target RASS 0 to – 1.

Preparation

- Currently available: 1 ml = 100 mcg
- Give IV Bolus: 0.5 ml – 1 ml
- Add 2 ml Dexmedetomidine with 48 ml NS in 50 ml Syringe pump, so 50 ml = 200 mcg, 1 ml = 4 mcg

- Start infusion at 0.2 mcg / Kg / hr. = 3 ml / hour for 60 kg (12 mcg)
- Reassess over 5 mins and Increase Infusion by 3 ml / hour
- Maximum infusion rate: 1 mcg / Kg / hr. = 20 ml / hour for 60 kg (60mcg)
- Doses Used: 3 / 6 / 9 / 12 / 15 ml/hour – DO NOT USE at other infusion rates.
- Titrate down the infusion rate and maintain at that rate when target RASS is achieved

5.3 Protocol for Delirium Monitoring and Management

Every patient admitted to an adult ICU will undergo routine sedation and delirium assessment using standardized, validated assessment tools.

• A nurse should perform and record the results of the Richmond Agitation and Sedation Scale (RASS) every 2 hours with Vital Signs. See Appendix for RASS Score.

• A Nurse should perform and record the results of the Confusion Assessment Method-ICU (CAM- ICU) twice a day or Intensive Care Delirium Screening Checklist (ICDSC) and whenever a patient experiences a change in mental status. See Appendix for CAM ICU and ICDSC.

• Each day during rounds, the team should set "target" RASS score for the patient to be maintained for the following 24 hours.

• Each day during interdisciplinary rounds, the nurse should inform the team of the:
  - Patient's "Target" RASS score
  - Patient's actual RASS score
  - Patients CAM-ICU status or ICDSC Score
  - Sedative and analgesic medications the patient is currently receiving

5.3.1 Non-pharmacologic methods for Prevention of Delirium

• Ensure Daily Awakening Trials is performed

• Continually reorient patient to environment/surroundings

• Perform Early mobilization:
  - Out of Bed and Wheelchair Mobilization for All
  - Ambulation if OFF Inotropes AND Low Ventilator Settings i.e. PEEP < 8 and FiO_2 < 50%

• Promote effective sleep/awake cycles

• Perform timely removal of catheters/physical restraints

• Ensure the use of eyeglasses, hearing aids

• Minimize continuous noise/stimulation at night

• Daylight exposure and orientation to Day and Night

• Minimize benzodiazepine for sedation – Consider Alcohol Withdrawal States in Chronic Alcohol Consumers

5.3.2 Pharmacologic treatments of Delirium

Consider Using Following Medications for Management of Delirium

<u>i. Haloperidol:</u>

• IV 5 mg Bolus repeat every 3 – 5 mins till agitation settles down.

• Calculate the total dose required and divide into q 6 hourly standing doses for few days

ii. Quetiapine:

• Tab. Quetiapine 25 mg BD / TDS and Increase dose as required.

iii. Olanzapine:

• Tab. Olanzapine 10 mg BD / TDS

Consider daily ECGs and look for QT prolongation in patients on these drugs.

5.4 Nutrition in Critically Ill Patient

A. Enteral Nutrition

• All ventilated patients must receive an orogastric tube and NOT Nasogastric Tube

• Start early feeding i.e. within 24 - 72 hours of ICU admission

• The correct position of the tube should be confirmed by either Injecting 10-20 ml of air down the tube and auscultating the epigastric area or with a Radiography (X-Ray)

• All patients receiving feeding must be placed in the semi-recumbent position with the head of the bed elevated to 45 degrees.

•Enteral feeding for patients who have undergone recent abdominal and bowel surgeries may require prior discussion with the surgeon before commencement.

• Patients should preferably receive continuous feeding during the acute phase. They can be switched to intermittent bolus technique later.

• Volume Based Feeding Schedule is preferred.

• Set start rate and target rate before commencing the enteral feeding.

• Total Calorie Required: 30 ml / kg of Actual Body Weight
  - Start with 50% of required Calorie
  - Built up to 80% of the Target Calorie over 72 hours
  - Do NOT Overfeed, Neither Volume, nor Calories

• Total Protein Required: 1.5 – 2 gms/ Kg per day
  - Add Protein Supplement (PS) Powder in Each Feed to meet the requirements.
  - Whey based protein has high protein content i.e.; 10 gms protein supplement powder = 7 gms protein

Intermittent Bolus Enteral feeding

• Start with 50ml Dextrose Normal Saline every 2 hours for three times.

• Progress to other Liquid diet / Blended Tube Feed (Calorie Diet from Nutrition Department or commercially available Balanced Nutritional Supplement - BNS) after the three DNS feeds is tolerated.

• Low Volume Feeding is recommended.
  - 200 ml or Less in Each Feed
  - At Least 10 Feeds for 24 hours

• Aspirate every 6 hourly ONLY (At Times: 00:00, 06:00, 12:00, 18:00)

- If Aspirate <500 ml return aspirate to patient. Increase by 50 ml after every feed till caloric needs are met.
- If Aspirate > 500 ml, (called as - High Gastric Residual Volume); AND/OR if the patient reflux, the stomach should be emptied, feedings held for 2 hours, and then reduce rate by 50% of initial bolus.

• Use Naso-Jejunal Tube for Feeding in Patients with Feeding Intolerance, High Gastric Residual Volumes and in Acute Pancreatitis

• Use Motility agents if Required: Motility Agents to be used in patients who experience feed intolerance (high gastric residuals, emesis).

- IV Metoclopramide 10-20mg 6-8 hourly and/ Or
- PO/NG Erythromycin 125 mg QID or 250 mg QID

Continuous Enteral Feeding

• Feeding Pump is required.

• Start at 25 to 30 ml/hr. and increase by 10 to 25ml/hr. every six hours as tolerated (i.e. Gastric Residual Volumes < 500 ml) until caloric goal is achieved.

• Aspirate the feeding tube every 6 hours.

• If Aspirate > 500 ml, (and/or should the patient reflux), feedings should be held for 2 hours, and then reduce rate by 50% of initial rate.

• Exclude bowel obstruction first if there is no clinical evidence of bowel obstruction, administer prokinetic agents. (Metoclopramide, Erythromycin).

• Once further aspirates are < 500 ml follow continuous feeding protocol.

• If aspirates continue to exceed 500 ml after the above has been carried out, consider the use of small bowel feeding

• Monitor nutritional adequacy (volume of EN received in last 24-hour period/prescribed 24-hour volume) daily and report percent intake on daily rounds.

• Flush tube with at least 10 mL sterile water every 4 hr. (q 4 h) during feedings, at beginning and end of feedings, after aspiration for residuals, and before and after medication administration.

B. Total Parenteral Nutrition (TPN Protocol)

Pre-requisite for TPN

• Confirm the correct location of central venous catheter (CVC) before initiating total parenteral nutrition (TPN). The tip of the CVC should be in the vena cava or the axillary or subclavian veins.

• Because of high infection risk and compatibility issued, TPN is infused only through a dedicated lumen. Designate one port exclusively for TPN if a multi-lumen catheter is used to administer parenteral nutrition.

• Label the lumen used for TPN to ensure that it is not used for other medications/fluids.

• A physician must order TPN daily using the appropriate TPN order calculation.

• A solution that is to be delivered peripherally should have an osmolality below 900 mOsm/kg to avoid irritation to the blood vessels.

Care during TPN Administration

• Prepare all TPN connections with alcohol swabs vigorously for 10 seconds prior to entering.

• IV set should be changed every 24 hours.

• TPN should always be infused via an infusion pump.

• For sudden/unexpected cessation of central TPN, infuse a dextrose-containing solution (D5W) at the same rate for at least 4-6 hours or until new TPN is started (especially in patient on Insulin or prone to hypoglycemia).

• Patients with malnutrition, malabsorption, wasting syndromes such as cancer, prolonged fasting, or chronic alcoholism will require additional supplementation of thiamine, electrolytes, and zinc on commencement of parenteral nutrition to reduce the risk of developing re-feeding syndrome.

Caution

DO NOT:

•Administer medications concurrently or intermittently into the same lumen as TPN.

• Initiate TPN through a lumen that has been used for any other purpose

• Add medications to TPN bag.

• Administer glucose concentration > 10% via peripheral line in adults.

Assessment/Monitoring

• Assess for signs/symptoms of catheter-related complications every shift.

• Send for labs as ordered. See lab order sets for patient on TPN attached herewith.

• On duty doctor should be informed of following and actions to be taken:

- Nausea and Vomiting
- Blood glucose: >180 mg/dl, <70 mg/dl
- Signs/symptoms of infection (systemic or at IV site)
- Sudden/unexpected cessation of TPN
- Dislodgment of central venous access device

Table 12: Monitoring Patients on Parenteral Nutrition

Parameter	Initial	Stable
Nutrient intake from oral, enteral, or parenteral nutrition	Daily	2X week
Fluid Balance Charts	Daily	Daily
Weight	Daily	Daily
Temperature, blood pressure, pulse, respiratory rate	Hourly	4-6 hourly

Hang-time

- The maximum time for a lipid only solution bag to hang is 12 hours.
- The maximum time for three-in-one or two-in-one solution bag to hang for is 24 hours.
- Any remaining solution should be discarded.

Regimen

Continuous Parenteral Nutrition

Parenteral nutrition infuses for 24 hours continuously. Infusion rates usually range between 50-150mL/hr. This is the preferred and most commonly used regimen.

Cyclic / intermittent nutrition

Parenteral nutrition is run over a shorter period and then stopped. The shorter the period of nutrition, the higher the rate may need to be to meet the patient's requirements. Rate as high as 300ml/hr can be used. Increases the risk for hyperglycemia and volume overload.

Starting parenteral nutrition

- Actual measued weight should be used if the patient is underweight or normal weight.
- In overweight/obese patients, adjusted body weight should be used as a guide to estimating nutritional requirements
- Calculate the total nutrition requirement, including calories and target infusion rate.
- Usual calorie requirement is 25 – 30 kcal/kg/day.
- Do NOT add calories from protein when calculating calories.
- Start the infusion slowly at 50% of the target infusion rate for 1 to 2 hours.
- Increase to target infusion rate after 1- 2 hours of starting infusion.
- Infuse total calculated volume over 24 hours.
- Include PN volume in calculating Total Fluid Intake and make sure patient is not volume over-loaded.
- Hypocaloric PN dosing (≤20 kcal/ kg/d or 80% of estimated energy needs) with adequate protein (≥1.2 g protein/kg/d) should be considered in appropriate patients (high risk or severely malnourished) requiring PN, initially over the first week of hospitalization in the ICU.
- Where there is no obvious risk of refeeding syndrome or other metabolic issues, TPN can be commenced at the target infusion rate as long as measures have been taken to minimize metabolic complications and appropriate monitoring (including hourly blood glucose monitoring for the first few hours) is in place.

• Starting the infusion at half the goal infusion rate for an hour or two, before increasing to goal rate, can prevent hyperglycemia, and is recommended in patients with known glucose intolerance.

Tapering and Discontinuation

• As tolerance to EN improves, the amount of PN energy should be reduced and finally discontinued when the patient is receiving >60% of target energy requirements from EN.

• If the patient is not on insulin therapy, decrease the PN rate by 50% and continue to infuse for 1-2 hours before discontinuing.

• When discontinuing PN, it is important to monitor for hypoglycaemia.

• For patients on an insulin infusion or subcutaneous insulin, more care needs to be taken when ceasing PN. Insulin dosing will need to be adjusted accordingly.

Sending Laboratory Tests in patients with TPN

Hold Parenteral Nutrition for 10 minutes before drawing all labs and avoid contamination of the drawn blood with TPN.

Table 13: Laboratory test in patients with TPN

Blood Sugar	• Hourly until stabilizes, then 4-6 hourly • Hourly if on insulin infusion
Na, K	Daily
Urea, Creatinine	Baseline then 2 X week
Mg, Ca, PO4	Baseline then 2 X week
AST, ALT, ALP, Bilirubin, INR, aPTT	Baseline then 2 X week
Lipid profile	Baseline, on 3rd day then weekly
Iron profile, MCV, Vit B12, Folate	Baseline then as required
TC, DC, CRP, ESR, Albumin	Baseline then as required

5.5 Protocol for Prophylaxis of Venous Thromboembolism/Deep Vein Thrombosis (DVT)

• On admission to the intensive care unit (ICU), all patients should be assessed for their Risk of Venous Thromboembolism (VTE) also known as Deep Vein Thrombosis (DVT).

• Accordingly, most patients should receive thromboprophylaxis.

• Prophylaxis should be reviewed daily and changed, if necessary.

• Consider withholding the heparin product when there is a significant decrease of platelet count (50% of initial count) or decrease to less than 100,000/ml of blood or when INR > 1.5.

• Check platelets at least q 3 days while on Heparin.

5.5.1 Drugs

• Low Dose unfractionated heparin (LDUH, UFH) e.g. Subcutaneous (S/C) Heparin 5,000 units 12 hourly.

• Low molecular weight Heparin (LMWH) e.g. S/C Enoxaparin 40 mg daily when Creatinine Clearance greater than 30ml/min or 30 mg daily when Creatinine Clearance less than 30ml/min.

5.5.2 Non-Pharmacological

• Pneumatic Sequential Compression Devices (SCDs) must be used for patients in whom Heparin is contraindicated. But Prior to use of SCD, doppler of leg veins shall be performed.

• TED Stockings has NO ROLE in DVT/VTE Prophylaxis and should not be used in ICU for VTE Prophylaxis.

5.6 Protocol for Use of Vasopressors and Inotropes

5.6.1 Target for Blood Pressure Management

• Ensure adequate fluid resuscitation prior to initiation of Vasopressor/Inotrope. 'FILL THE TANK.'

• Remember, FLUID BOLUS = 1 L NS over 15 mins

• Target SBP > 90 mmHg, DBP > 55 mmHg

• Target MAP > 70 mmHg

• If Target MAP is not reached, Escalate (Increase) Vasopressors/Inotropes: Every 5 min

• Once Target is reached, De-escalate (Decrease) Vasopressors/Inotropes: Every 30 min

• Acceptable change: +/- 10 mmHg of MAP

5.6.2 Drugs used for Vasopressors / Inotropes in ICU:

<u>iii. Dopamine and Dobutamine</u>

• Preparation: Body weight x 3 in 50 ml in NS/D5W

• Preparation: Body weight x 6 in 100 ml NS/D5W

• Then, ml/hr. = mcg/kg/min; e.g. 5 ml/hr. = 5 mcg/kg/min

• Dose: 5 - 20 mcg/kg/min

• Use in dosage: 5/7.5/10/15/20 mcg/kg/min

• Route: Peripheral/ Central line (Most Distal Port)

<u>iv. Vasopressin</u>

• Preparation: 40 units (2 ampoules) in 40 ml NS

• Route: Central line (Most Distal Port)

• Dose: 0.03 Units/min, i.e. 1.8 ml/hr.

• No Tapering of Vasopressin. Either ON or OFF.

v. Phenylephrine

• Preparation: 10 mg in 100 ml NS, so 1 ml = 100 mcg

• Route: Central line (Most Distal Port) or Peripheral Line

• Dose: Bolus - 50 to 100 mcg every 1-2 min for resuscitation of shock, management of hypotension as Rescue drug (during procedural sedations, transfer, etc.)

• Infusion: 0.5 - 5 mcg/ kg/ min

vi. Noradrenaline and Adrenaline

• Preparation: 4mg in 50 ml NS/D5W or 8 mg in 100 ml NS/D5W

• Dose: 0.01- 0.3 mcg/kg/min

• Route: Central line (Most Distal Port)

• Dose chart can be used which gives ml/hr. based on body weight and adjust the weight to the nearest number.

6. Nursing Care of ICU Patients

Purpose

The purpose of this clinical guideline document is to help critical care nurses to provide standard care to a patient in ICU. The patient may be on endotracheal tube (ET tube) or tracheostomy tube (TT). Nursing care of the patient is of paramount importance for the better outcome of patients minimizing risk of complications. This chapter describes the important aspects of nursing care in mechanically ventilated patients based on current knowledge in the available literature and recommendations from different Critical Care Societies.

Nursing Interventions mainly consist of

a. Performing 5 moments of hand hygiene

b. Application IPC measures according to task

c. Development of individual patient nursing plan

Nurses must perform regular hand hygiene and don appropriate personal protective equipment (PPE) and obtain all care and plans during handover at the start of shift duty.

Objectives

Provide quality nurse management of the Critically Ill Patient in the following areas:

- Constant Monitoring
- Respiratory Care
- Cardiovascular care
- Gastrointestinal care
- Nutritional care
- Neuromuscular care
- Comfort and reassurance
- Communication within the ICU team

- Fluid, electrolyte, and glucose balance
- Bowel and bladder care
- Dressing and wound care
- Communication with patient and relatives

1. Constantly monitoring the parameters of the patient using an ICU monitor:

The medical condition of the critically ill patient may deteriorate rapidly, for this reason it is imperative to ensure continuous monitoring of the patient's status using specialize ICU equipment.

- Maintain parameters within given range
- Monitor and document parameters on an individual patient ICU (NEWS) chart
- Attention to alarm settings, should not be set to 'off'

A. Maintaining Airway

Continued safe positioning of the endotracheal tube is imperative to maintain the patient's airway, prevent buccal, oropharyngeal, and tracheal trauma from the tube and cuff. Correct inflation of the cuff is necessary to reduce the risk of secretion aspiration into the lung and to decrease the risk of ventilator associated pneumonia (VAP). The aim is to improve the patient's oxygenation:

- Assess respiratory rate and depth, inspect thorax for symmetry of movement.
- Observe for signs of cyanosis
- Continuously monitor pulse oximeter
- Elevate head of the bed 30-45* degrees
- Suctioning for airway clearance.
- Chest physiotherapy and breathing exercises for secretions mobilization.
- Humidification of airway through the ventilator to help liquefy the secretions for easy removal.
- Use bronchodilators and mucolytic agents.

B. Maintenance of Endotracheal tube (ETT)

- Secure endotracheal tube in position and document position of tube at incisor teeth level; also provide support to the ETT and tubing as needed.

- Perform oral hygiene by providing good oral care with Chlorhexidine solution 0.2%. After each cleansing, apply a mouth moisturizer to the oral mucosa and lips to keep tissue moist.

- Subglottic suctioning with low negative pressure. (-20 to 30 mm Hg).

- Endotracheal tube (ETT) or tracheostomy tube (TT) suction is necessary to clear secretions and to maintain airway patency, and to therefore optimize oxygenation and ventilation in a ventilated patient.

- After oral hygiene is completed, change the ETT securing mechanism with new tape, ties, as needed.

- Ensure proper cuff inflation and check it six hourly to maintain the cuff pressure at 20-30 cm H_2O.

- Heat and moist exchange (HME) filter should be changed if it gets soiled or in every four days.

• Do not change the ventilator tubing on a regular basis. Only change the ventilator tubing when soiled or mechanically malfunctioning.

• Hand hygiene and other Infection Control and Prevention (IPC) practices should be followed.

C. Suctioning

Following are the important steps to follow.

• Hand Hygiene and appropriate PPE

• Turn on suction apparatus and set vacuum regulator to 80-120 mm Hg.

• Monitor the patient's cardiopulmonary status before, during and after the suctioning period.

• Hyper oxygenate the patient for at least thirty seconds using hyperoxygenation button or pressing FiO2 100%.

• Suctioning is done only when indicated.

-Use close suctioning only; insert the catheter into the artificial airway until resistance is met, then pull back 1-2cm before applying suction. Flush the in-line suction catheter with sterile solution after completion of ET/TT suctioning.

-Open Suctioning technique is also available, but it should not be practiced because the risk of infection is very high in open suctioning technique.

D. Check Ventilator Settings and Modes

• Check oxygen saturation, tidal volume delivered, I: E ratio, RR, PIP etc. Serial monitoring is important to detect change early.

• Check whether the set modes and settings are appropriate for the patient or not.

• Listen to the breath sounds and note if there are any changes from previous settings.

2. Meet Nutritional demands of the patient

In critical care, malnutrition has a significant, negative impact on a patient's ability to respond to medical treatment. Enteral nutrition is known to counteract the metabolic changes associated with critical illness that increase the risk for serious complications and poor clinical outcomes.

It is essential to find approaches that enhance early delivery of enteral nutrition that meets requirements and supports improved outcomes. Nurses are in a unique position to take an active role in promoting the best nutritional outcomes for their patients by using and evaluating nutrition support protocols.

• Initiate enteral nutrition (EN) within 24-48 hours following the onset of critical illness and admission to the ICU and increase to goals over the first week of ICU stay.

• Take steps as needed to reduce risk of aspiration or improve tolerance to gastric feeding (use prokinetic agent, continuous infusion, elevate the head of bed).

• Implement enteral feeding protocols with institution-specific strategies to promote delivery of EN.

• Do not use gastric residual volumes as part of routine care to monitor ICU patients receiving EN.

• Start parenteral nutrition early when EN is not feasible or sufficient in high-risk or poorly nourished patients.

• Current guidelines support using a simple weight-based equation (25-30 kcal/kg daily) to determine energy requirements for most ICU patients.

- Start with 50% of required Calorie
- Built up to 80% of the Target Calorie over 72 hours

• Protein requirements range from 1.5 to 2.0 g/kg actual body weight per day.

3. Maintaining Safety

• Follow measures to prevent cross infection and nosocomial infection.

• Maintain adequate body temperature.

• Put side rails on patient bed.

• Provide mental, and emotional support, talk to the patient, unconscious patients can still hear.

• Visiting hours should be defined and allow verbal communication for those who are able to communicate.

4. Communication

• Explain all nursing/medical procedures in advance of performing them.

• Assess the ability of the ventilator dependent patients to communicate.

• Use nonverbal methods of communication and be alert to nonverbal clues.

• Use signals, signs, nodding, palms writing, lip reading; provide paper and pencil, magic slate.

• Allow patient to respond if able to, and repeat explanations.

• Ask simple yes/no questions to which she/he can nod or shake head.

5. Maintaining Skin Integrity

• Regular changing in position at least 4 hourly or according to needs

• Passive exercises

• Prevent foot drop

• Massage of appropriate body parts

6. Maintaining Corneal Integrity

Unconscious patient may lie with their eyes open & have inadequate or absent corneal reflexes.

• Perform regular eye care using aseptic technique

• Apply eye drops regularly

• Attend to periocular edema

• Maintain natural eye moisture by keeping eyes closed using tape if necessary.

7. Promoting Sensory Stimulation

- Maintain the sense of daily rhythm
- Maintain the same schedule each day
- Orient the patient regularly
- Tactile contact is important proper communication, in a language that is known to the patient.
- Always address the patient by preferred name and explain the procedure each time.

8. Supporting the family

If the patient is unconscious, family members may show anger or anxiety. This can be reduced by:

- Regularly update the next of kin according to protocol
- Reassure next of kin that they will be contacted in case of emergency
- Encourage visitors to talk to the patient even though the patient may not be responsive
- Show relatives how to perform basic care e.g. eye care, passive exercises, etc. where appropriate so they feel more involved

9. Attaining Self Care

Where appropriate encourage the patient's independence to perform simple tasks:

- Teach
- Support
- Encourage and supervise activities until the patient gains independence.

10. Care Bundles in Intubated patients are described in chapter 5.

11. Nursing Considerations on Prone patient

Apart from the routine care of the patient on mechanical ventilation, care for a patient who is in prone position, the following safety check should be conducted:

- Perform bed safety area checks and patient assessment.
- Assess airway, endotracheal placement, and ties, ensure mouth care has been performed, check for pressure areas on lips and ensure the endotracheal tube is moved once per shift to minimize the risk of injury.
- There should be safe placements of all central venous catheters, arterial catheters, urethral catheter, nasogastric tubing, drain tubes.
- Check the central venous catheters, arterial line, and peripheral line site for any signs of infection as per the hospital.
- Lines inserted in the upper torso are aligned with either shoulder, and the excess tubing is placed at the head of the bed. Chest tubes and lines placed in lower torso are aligned with either leg and extend off the bed.

- Care must be taken to avoid any types of accident like tube dislodgement, the risk is very high in prone positioning.
- Positioning must be carried out two hourly with use of a small blanket fold, and positioning of the hands must be changed every two hours in swimmer's position one up and one down.
- Feeding must be continued through Orogastric tube if intubated.
- There is high risk of developing pressure sores on different parts of the body; care must be taken to regularly monitor high risk points, ears, basal scull, sacrum, elbows, heels etc.
- Provide frequent oral care, including applying lip balm and suctioning of the airway as required.
- Maintain eye care to prevent corneal abrasions, eyes may be lightly taped closed if necessary.

7. Long Term Outcome and Quality of Life

Outcomes after ARDS are similar to those of other survivors of critical illness and largely affect the nerve, muscle, and central nervous system but also include a constellation of varied physical devastations ranging from contractures and frozen joints to tooth loss and cosmesis.

Compromised quality of life is related to a spectrum of impairment of physical, social, emotional, and neurocognitive function and to a much lesser extent discrete pulmonary disability.

Intensive care unit-acquired weakness (ICUAW) is ubiquitous and includes contributions from both critical illness polyneuropathy and myopathy, and recovery from these lesions may be incomplete at 5 years after ICU discharge.

Cognitive impairment in ARDS survivors ranges from 70 to 100 % at hospital discharge, 46 to 80 % at 1 year, and 20 % at 5 years, and mood disorders including depression and post-traumatic stress disorder (PTSD) are also sustained and prevalent.

8. Care of the Terminally Ill Patient/ End of Life Care

In critically ill patients who are unlikely to recover, and death is imminent, the ICU team should ensure that the patient is cared for and dies in a dignified and pain free manner, with as little suffering as possible and if possible in the presence of their loved ones.

- If a patient is terminally ill, medical practitioners need to consider which treatments may offer benefit to the patient or if treatments will cause discomfort or harm.Consideration should be given to the administration of CPR and other life-saving resuscitation measures adopting a case by case approach, and the family should be informed and advised if the patient is deemed as terminally ill or unlikely to benefit from this intervention. Palliative care should be provided to ensure that the patient remains comfortable and pain free.

• If it becomes clear when caring for a terminally ill patient that the treatment isn't working and that any treatment that is not palliative in nature is futile, e.g., terminally ill patient admitted in ICU with ventilator support, medical practitioners should discuss the situation empathically with the patient's family as soon as possible regarding discontinuation of life supportive measures keeping in mind the best interest of the patient.

• In ICU, most patients are very sick and their medical condition can deteriorate rapidly. Individual cases should be reviewed daily and changes in the patient's resuscitation code status should be recorded and clearly documented using the standard code status, in the patients notes and communicated efficiently to all health staff in the ICU.

• While taking care of patients, we need to be clear on the understanding of the following code status terminologies which are commonly used in health facilities in Nepal:

- Full code: Full code means that the patient shall be offered all the available treatments possible. If certain treatments or modalities are not available in that ICU, the patient's family should be informed of the various treatment options and modalities available.

- Do Not Resuscitate (DNR): DNR does not mean Do Not Treat. It actually signifies refusal of administration of "Cardio Pulmonary Resuscitation (CPR)" in case of sudden cardiac arrest. Hence all the required treatment should be continued as usual except the CPR (chest compression, airway management, defibrillation, and administration of drugs for cardiac arrest).

- Do Not Intubate (DNI): DNI means not to perform endotracheal intubation and not to perform artificial mechanical ventilation by an endotracheal tube in a patient even if needed. But all other treatment modalities should be continued including High flow oxygen therapy or Non-Invasive Ventilation including CPAP, BiPAP.

- DNR/DNI: This combined term is commonly used (DNR/DNI), that means the patients should not be intubated and chest compression, defibrillation and/or Manual Ventilation should not be offered. All other medical managements including IV medications, pain management, hypoglycemia and arrhythmia management should be continued even in these DNR/DNI patients.

- Do Not Escalate (DNE): DNE is a term used when patient is terminally ill and the treatment deemed ineffective but the family is not able to make decision about with drawal of active life support. With this DNE order, the treatment will be continued as is while there will be no escalation in the level of treatment including titration of vasopressors dosage, oxygen requirements, and other modalities of treatment (dialysis, ECMO) would not be offered.

- (DNT): DNT is commonly used when a patient is terminally ill and the treatment is deemed ineffective and so further treatment is discontinued. Under these circumstances, written consent to stop all ongoing medications and treatments for the patients is required. However, pain medicines, IV fluids and feeding shall be continued.

- Withdrawal of Active Life Supporting Treatment (WALST): Withdrawal of active life supporting treatment is done when the treatment is deemed inappropriate and the patient is unnecessarily suffering because of prolonging life by artificial means. After detailed discussions and explanations to the family members, the family members have

to sign a WALST consent. Such discussions should involve as many family members as possible so that there is family agreement to the decision accepting the withdrawal of life support.

Under these circumstances, all efforts should be made to ensure the patient is kept as comfortable as possible, with use of medication if necessary, and artificial life support and treatments should be stopped including detachment from any mechanical ventilation. Patients can be kept on a T-piece for some time or even extubated on room air based on the institutional practice and level of patient comfort. Patients may be given morphine as IV bolus or in continuous infusion in case of pain or discomfort. Withdrawal of active life support should be discussed with the senior ICU Consultant and carried out by senior ICU nurse who has experience in handling such terminally ill patients. Even after withdrawal of life support, all nursing care procedures should be continued including regular positioning, whole body care, physiotherapy, IV fluids, feeding and administration of analgesic medicines.

• Euthanasia, the act of painless killing of a patient suffering from an incurable and painful disease, is not legalized in Nepal and hence must NOT be practiced.

9. Rehabilitation in ARDS

Rehabilitation interventions in ARDS is expected to contribute to reduction in the, a) length of stay in critical care and in hospital; b) hospital readmission rates; c) improvement in the quality of life for people etc. Rehabilitation measures include physiotherapy, occupational therapy, speech & language therapy, clinical psychology, medical social work etc.

In Nepal, physiotherapists are available in most tertiary hospitals and their role is crucial in improving chest clearance in ICU, breathing patterns, early mobilization and for maintaining and restoring muscle & joint functions. Since other rehab disciplines are in scarcity and are scattered, a trans-disciplinary approach may be used where a physiotherapist can be trained to provide basic interventions from other disciplines as well and/or identified and referred to relevant rehabilitation specialty for further management. Rehabilitation goals should be individualized, patient-centric, and have short-, medium- and long-term goals developed in consultation with the support of the treating doctor/physician.

For example, in the critical care unit, reduced mobility, weakness and fatigue will be the main problems, for which the overall goal will be early mobilization. A short-term goal might be for the patient to be able to sit on the edge of the bed with support, a medium-term goal to stand aided and a long-term goal to march on the spot or take a few supported steps. Later in the ward, patient may continue to have reduced mobility but the goals will change; a short-term goal might be to walk to the toilet and a long-term goal to manage the stairs before discharge.

Rehabilitation in the ICU

• For patients requiring artificial ventilatory support and are intubated:

Physiotherapy referral may be given to facilitate chest clearance. Physiotherapist should be cautious when giving chest physiotherapy, and should constantly monitor the vital parameters of the patient e.g. SpO_2 and to work in close consultation with the treating physician/doctor.

• For patients who are not intubated: Chest physiotherapy in terms of breathing exercise, coughing, sputum clearance, increasing vital capacity with incentive spirometer may be referred by the treating physician/doctor.

Mobilization Therapy

• This may be referred by the treating physician and the physiotherapist can encourage patients on ventilators to participate in range-of-motion or resistance activities, sitting, or standing. It may be necessary to reduce sedation to allow patients to participate. Mobilization therapy is associated with fewer ventilator days and a greater likelihood of being able to walk at hospital discharge.

Identification of patient at risk

• Patients with ARDS are at risk of developing physical and psychological morbidity and need comprehensive assessment to identify rehabilitation needs early to facilitate prompt management.

• The following patients are at risk of psychological morbidities, and the treating physician should send a physio/rehab referral within 4 days of admission to critical care or before discharge from critical care whichever is earlier.

- Unable to get out of bed independently.
- Anticipated long duration of critical care stay
- Obvious significant physical or neurological injury
- Lack of cognitive functioning to continue exercise independently
- Unable to self-ventilate on 35% of oxygen or less
- Presence of premorbid respiratory or mobility problems
- Unable to mobilize independently or perform basic hygiene functions

Rehabilitation in the ward/Physiotherapy department

The treating physiotherapist should perform a comprehensive clinical assessment to determine the rehabilitation needs of the patients including ADL/functional assessment to assess the patient's daily functional ability. Based on that, s/he can develop,

- short-term rehabilitation goals - for the patient to reach before they are discharged from hospital.
- medium-term rehabilitation goals - to help the patient return to their normal activities of daily living after they are discharged from hospital.

• Common problems to address include, symptoms related to dyspnea, secretion retention, and decrease aerobic capacity. Other non-respiratory symptoms include, muscle loss, muscle weakness, musculoskeletal problems including contractures, respiratory problems, sensory problems, pain, and swallowing and communication problems.

• Psychological challenges may include, emotional and cognitive dysfunction, in the absence of a multi-disciplinary team of experts, the PT can provide basic support and refer them to relevant rehabilitation professionals – e.g. clinical psychologists, speech & language therapists – elsewhere.

• A care pathway should be developed and shared for reference.

Cardio-pulmonary Rehabilitation

• The complication of ARDS related to lung capacity could last for more than 6 months to even few years. The quality of life is severely compromised and pulmonary rehabilitation would play a vital role in improvement.

• The pulmonary rehabilitation follows a graded exercise program targeting the endurance capacity of the patient, and physiotherapy skill techniques in improving lung volume and secretion removal should be continued.

• Assessment measures include, a six-minute walk test, Rate of perceived exertion (RPE), dyspnoea scores, etc.

Home Programme

• Discharge plans should be individualized and provide clear instruction for easing breathlessness, strengthening, flexibility, aerobic, and balance and posture exercises. The level of exercise depends on varying level of loss of functional ability based on ARDS survivors.

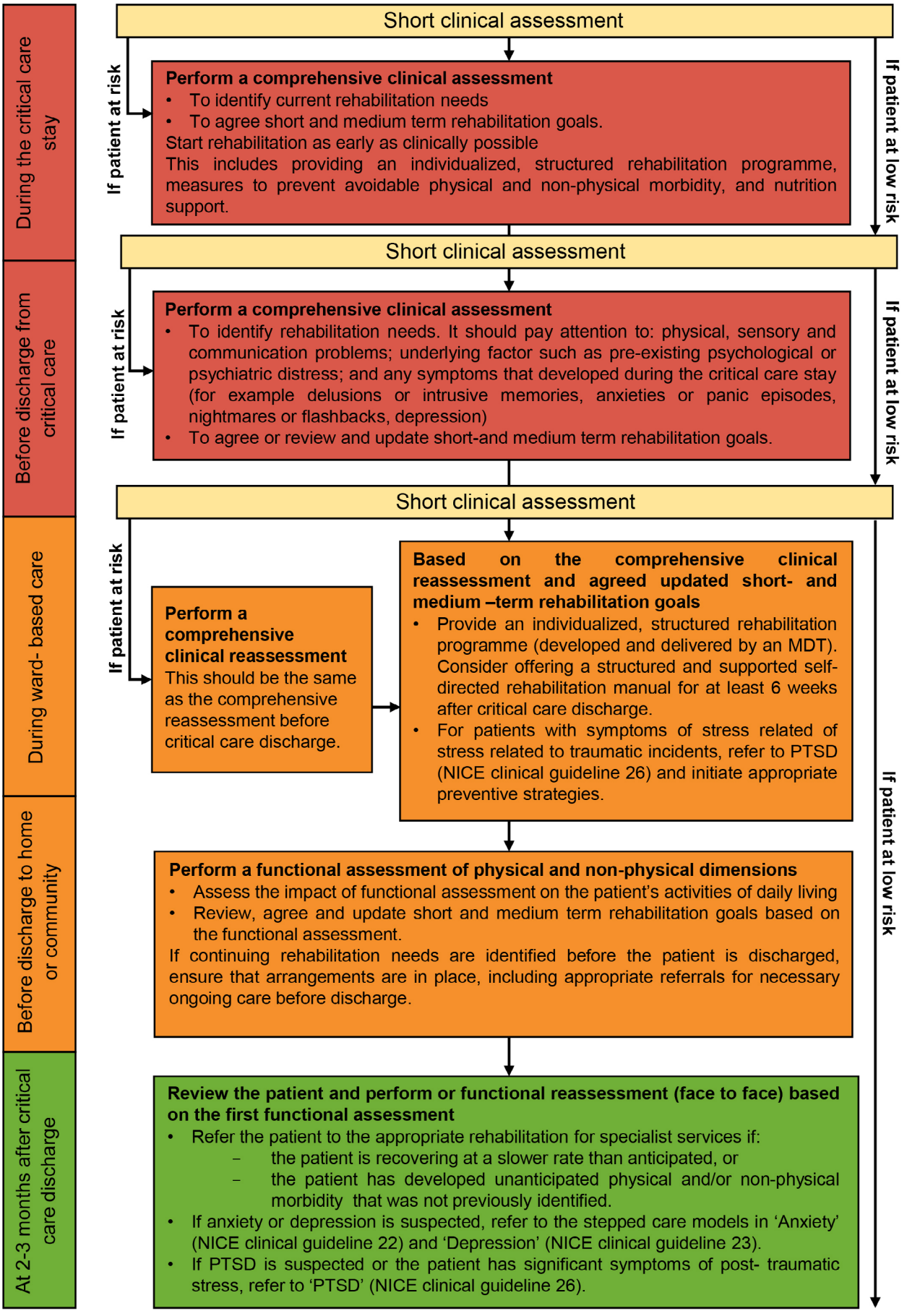
• Patients should be informed of the "Red flags" that require stopping of rehabilitation interventions and need an urgent medical review /referral these include:

- dyspnoea with minimal activity that does not improve with any of the positions for easing breathlessness
- chest pain, racing heartbeat, or experiencing dizziness in certain positions or during exercise or activity
- new onset of confusion or worsening confusion; difficulty speaking or understanding speech
- weakness in the face, arm or leg, especially in one side of the body; and/or
- anxiety or mood swings, altered level of consciousness, or suicidal thoughts.

Review / follow-up:

• Review patients with rehabilitation needs 2–3 months after their discharge from critical care.

• Carry out a health follow-up functional reassessment, and social care need, all of which should be recorded and documented. Titrate interventions and levels accordingly.



Flowchart 3: Care Pathway

10. Integrating Gender, Equity and Human Rights (GER) in Clinical Management (CM) of COVID-19

Gender, equity and human rights matter in health and clinical management. The men and women, girls and boys, or any individual of gender and sexual identity experience differences in health status, exposure to risk and vulnerability, access to and use of services, health-seeking behaviour, experiences in health care settings, and health and social outcome due to their biological and social standing in the society. Health inequities manifest in differential exposure, vulnerability, access, health outcomes and consequences, so it is very important to recognize these aspects and provide health services from gender, equity, and human rights perspectives. In response to COVID-19, the following aspects are suggested to strongly consider while managing COVID-19 patients in health facility settings.

1. Providing respectful care towards all patients

Naturally, we envision a relationship between patients and service providers characterized by caring, empathy, support, trust, confidence, and empowerment, as well as gentle, respectful, and effective communication to enable informed decision making. While dealing with the patients of COVID-19 and non-COVID-19 at clinical sites, health workers/providers need to be aware about the differences, providing fair treatment and respecting and protecting the rights of an individual. Health workers/providers need to:

- Demonstrate equal and fair treatment/behavior irrespective of an individual's age, sex, caste, ethnicity, socioeconomic status, education, sexual orientation, family/cultural background, disabilities or any other characteristics.

- Respect the right to information, informed consent and refusal; right to confidentiality, privacy, dignity, choices/preferences, equitable care; and self-determination; right to freedom from harm, ill treatment and discrimination; and right to timely healthcare and to the highest attainable level of health.

- Avoid unintended biases towards women, girls, (with or without disabilities) or any clients based on their identity and socioeconomic backgrounds.

- Be aware of social stigma and Dos and Don'ts. Refer the box -there are some dos and don'ts on language when talking about the COVID-19.

- Be aware of gender related biases, be non-judgmental.

- Be culturally sensitive and appropriate to age.

- Be aware of rights of childbearing women and respect those while providing care to them.

- Be aware on data for men and women on predisposing factors, delays in seeking care, co-morbidities for the COVID-19 and risk groups and link to diseases as well as possible biological differences in COVID-19 impact over men and women. Even though COVID-19 infections are distributed equally among men and women, evidence shows more deaths among men due to biological factors, resulting presumptively due to a more robust immune response among women.

• Be aware in regards with non-health effects of COVID-19 pandemic. Evidence suggests women have borne the brunt of non-health impacts, including job and wage losses, increases in unpaid work in homes including health work, increases in violence against women, especially intimate partner violence, and lack of adequate social protection. They have also faced lack of access to needed non-COVID-19 health services, especially sexual and reproductive health services.

Managing social stigma - Dos and Don'ts

DO– Use respectful and dignified verbal, and body language

Don't –Use offensive verbal and body language*

DO- talk about the new corona virus disease (COVID-19)

Don't- attach locations or ethnicity to the disease, e.g., "Chinese Virus".

DO- talk about "people who may-have COVID-19" or "people who are presumptive for COVID-19"

Don't- talk about "COVID-19 suspects" or "suspected cases".

DO- talk about people "acquiring" or "contracting" COVID-19

Don't talk about people "transmitting COVID-19" "infecting others" or "spreading the virus" as it implies intentional transmission and assigns blame.

2. Responding to gender-based violence (GBV)/violence against women and girls (VAWG)

The high prevalence of GBV/VAWG in Nepal is an ongoing challenge. NDHS 2016 reports 22% women experience physical violence. Global data show 1 in 3 women has experienced lifetime physical and/or sexual violence, mainly by an intimate partner. More importantly, available evidence points to significant increases GBV/VAWG increase in any emergency situation, and it has been exacerbated in COVID-19 situation and this has alarmed all actors working against GBV/VAWG.

The risks of violence that women and their children face during the current COVID-19 crisis cannot be ignored. "There never are excuses for violence". Health systems have an important role in ensuring that services for survivors of gender-based violence remain accessible during the COVID-19 pandemic. The routine screening of GBV is NOT recommended by WHO during COVID-19 response. WHO guidance includes the dos and don'ts to be followed in this regard. In case of a patient/client who comes to the health facility and discloses experience of violence, it is most important to respond.

What is gender - based violence (GBV)?

Gender based violence refers to harmful acts directed at an individual based on their gender. It is rooted in gender inequality, the abuse of power and harmful norms. GBV is a serious violation of human rights and a life-threatening health and protection issue. GBV is committed in many forms such as physical, emotional/psychological, sexual, cultural/social, economic or any kind that endangers the safety, health and well-being of an individual.

Domestic Violence refers to violent or aggressive behavior within home involving intimate partner and immediate family members.

Five Actions for Health workers/providers to respond to GBV/VAWG

• Be aware of the increased risk and health consequences of GBV/VAWG in the context of COVID-19.

• Recognize the signs and know when and how to ask about violence.

• If violence is disclosed, act to provide timely care for physical, sexual, reproductive and mental health.

• If violence is disclosed, provide First-line support and medical care to survivors. The first-line support is most important, and it involves 5 simple tasks of **LIVES**:

- **LISTEN:** listen to women, girls closely, with empathy, and without judging.
- **INQUIRE:** assess, identify and respond to person's various needs and concerns.
- **VALIDATE:** show that you understand survivor's experience, feeling and believe her.
- **ENHANCE SAFETY:** discuss a plan to protect the survivor from further harm if violence occurs again.
- **SUPPORT:** support her by helping her connect to information, services, and social support.

• Share information about available support, identify referral pathways and refer to other essential services.

Health facilities can identify and provide information about services available locally (e.g. hotlines, shelters, psychosocial counselling) for survivors, including opening hours, contact details, and whether services can be offered remotely, and establish referral linkages. It is important to understand women and girls of marginalised groups and with disabilities are likely to have additional risks and needs. WHO-National Federation of Disabled Nepal (NFDN), Yes We Can Project has set-up district level virtual help desk with woman peer counsellor to address the needs of women and girls with disabilities. The contact numbers are available on request from the National Coordinator of this project (nc@nfdn.org.np).

Remember: Safety, respect, confidentiality and non-discrimination in relation to GBV survivors and those at risk are vital considerations at all times.

3. Considerations for managers

Many women are at the forefront of the COVID-19 response. Study shows globally, women make up 70 per cent of the health workforce, especially as nurses, midwives and community health volunteers, and account of the majority of service staff in health facilities as cleaners, launderers and caterers. This scenario obtains in Nepal as well. Despite the large number, women are often not reflected in decision-making in response to COVID-19. Further, women are still paid less than their male counterparts and hold fewer leadership positions in the health sector and enjoy lower job security and social protection. Masks and other protective equipment designed and sized for men leave women at greater risk of exposure.

The lack of adequate attention to the menstrual hygiene needs of women health workers during long shifts is an added workplace-related challenge. So, Managers need to be aware of the above gaps and ensure from management aspect if the needs of women especially who are at forefront are prioritized and fulfilled. This means:

- The health care workers and caregivers have access to women/gender-friendly personal protective equipment (PPE) and menstrual hygiene products, i.e., the different sizes and also the design of the PPE needs to be made available and accessible considering the feminine and menstrual hygiene need.

- Flexible working arrangements need to be made to balance the burden of care specially for pregnant and breastfeeding mothers.

- Women health workers take the leadership and decision-making roles.

- Equal treatment and pay, paid leave and other social protection measures are ensured to women health workers in the public and private sectors.

4. Managing disaggregated data (Sex, Age and Disability disaggregation of data)

While the COVID-19 pandemic has affected everyone, women and girls (with or without disabilities), people from marginalised groups have been facing specific and often disproportionate economic, health, and social risks due to deeply entrenched inequalities, social norms, and unequal power relations. Therefore, understanding the gender-differentiated impacts of the COVID-19 crisis through sex and age, caste/ethnicity, disability disaggregated data is fundamental to policy and program responses that can reduce vulnerable conditions and build the agency of girls and women and marginalised groups placing gender and equity at their centre.

To manage the disaggregated data, the case reporting form of clinical management as well as vaccine monitoring form should include at least sex, age, disabilities, caste/ethnicity, co-morbidities, and health care worker status, and this should be reported in regular reporting system. Analysis by this disaggregation should be prioritized by the health facilities and higher levels to identify any gaps and develop priorities for interventions. The same can be used to analyse health inequities among different vulnerable groups, and to review, take appropriate actions and report periodically.

5. COVID-19 vaccination

There is a gender gap in COVID-19 vaccination. Evidence shows that in low-income countries, like Nepal women (with or without disabilities) have lower access to mobiles or digital devices

in comparison to men, as a result less women may face challenges in being able to register through online and digital portals for COVID-19 vaccination. Older women and people from rural, remote and urban poor households may be similarly disadvantaged. Similarly, women's typically lower levels of education and rates of access to radio, mobile, and/or internet or limited access to accurate and credible information can increase the risks of the spread of fear, rumors, and misinformation about vaccines reducing immunization uptake. And the same case might be for the elderly people.

For women, there are other factors that might act as barriers to access to timely and complete vaccination, such as women's care roles/ responsibilities and time poverty, decision-making power on health seeking and use of resources in households, lower education and literacy, limited mobility from access to safe transport and gender-related constraints on their ability to move about on their own, anticipated or perceived discrimination in health care settings, experience of harassment and violence etc. Older women may be particularly disadvantaged. Considering all these factors there needs to be ensured equitable access to vaccination:

- Compare the actual distribution of those covered by 1st and 2nd dose of the vaccine with the expected distribution, by age and sex of various eligible groups, if women and elderly prioritized for vaccine.

- Plan to offer vaccination to pregnant and lactating women in priority target groups.

- Be aware of the related barriers to vaccine enrolment/registration and follow-up.

- Use differentiated vaccine delivery strategies to effectively reach women, elderly and gender-diverse people. For example, in a few places, designated vaccine counters were set-up for persons with disabilities including accessible transportation to vaccine facilities.

- Monitor vaccine implementation progress and equitable access through selected priority indicators disaggregated data by sex and age, disability, and caste/ethnicity.

- Promote leadership and encourage participation of vulnerable groups in COVID-19 service delivery. For example, in Nepal, the groups of disabled people have taken leadership and participation in successful vaccine advocacy, data-driven advocacy, risk communication, access audits, identification of vulnerable household of persons with disabilities etc.

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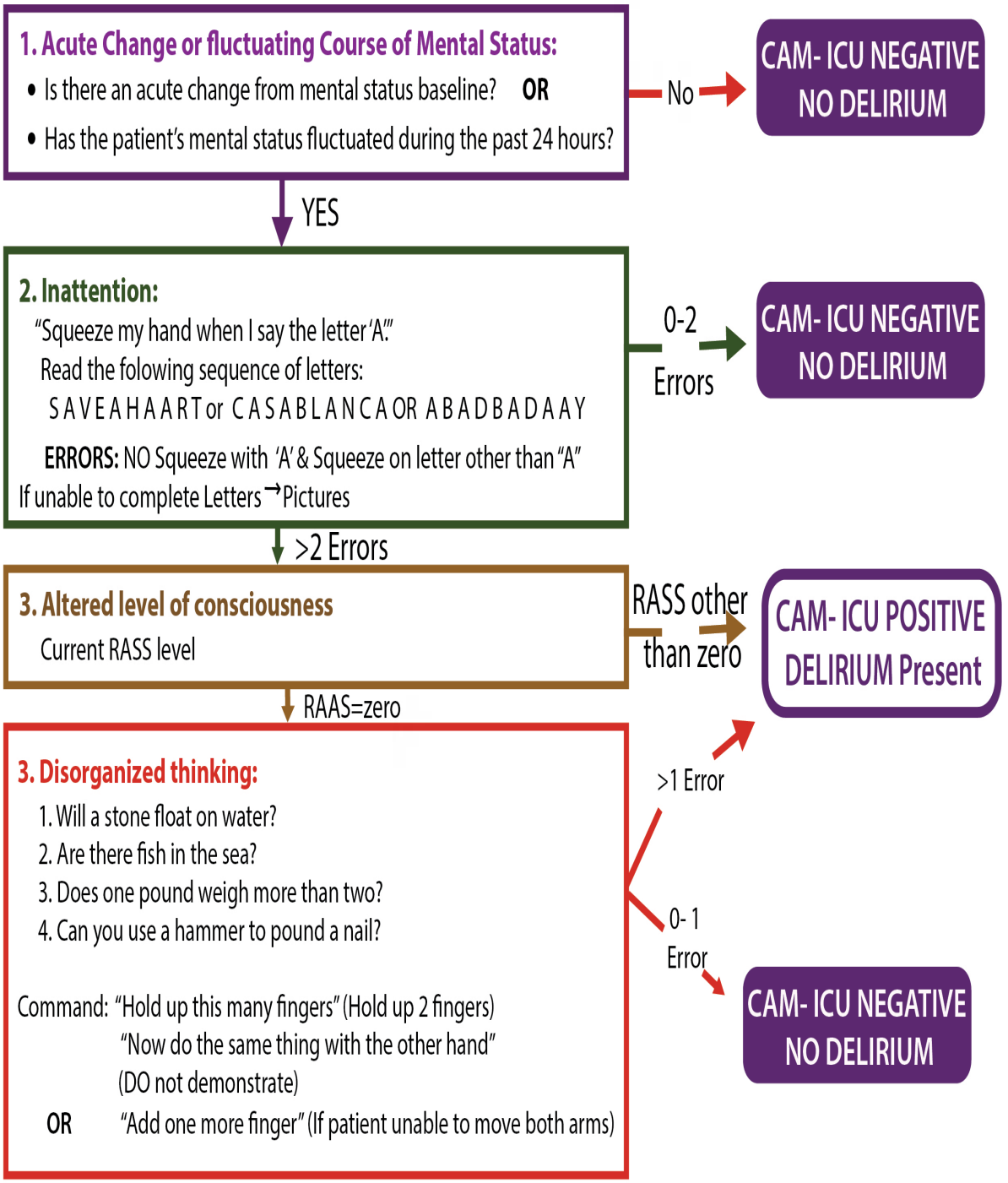
12. ANNNEX:

Annex 1: Richmond Agitation Sedation Scale

Score	Term	Description
+4	Combative	Overtly combative, violent, immediate danger to staff
+3	Very agitated	Pulls or removes tube(s) or catheter (s) aggressive
+2	Agitated	Frequent non-purposeful movement, fights ventilator
+1	Restless	Anxious but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained awakening (eye opening eye contact) to voice (>10 seconds)
-2	Light sedation	Brief awakens with eye contact to voice (<10 seconds)
-3	Moderate Sedation	Movement or eye opening to voice (but no eye contact)
-4	Deep Sedation	No response to voice, but movement or eye opening to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Annex 2 : Confusion Assessment Method for the ICU (CAM-ICU) Flow Chart



NOTES

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