COVID- 19 in elderly presentation

Pulmonary involvement and Management of Elderly Critically Ill patients with COVID-19 in ICU

Haleh Mikaeili

Associate Professor

Pulmonologist, Intensivist

Tuberculosis and Lung Disease Research Centre of TBZMED

General Considerations

Severe cases :

- hypoxemic respiratory failure
- acute respiratory distress syndrome (ARDS),
- septic shock
- cardiac dysfunction
- elevation in multiple inflammatory cytokines
- thromboembolic disease
- exacerbation of underlying comorbidities.
- In addition to pulmonary disease, patients with COVID-19 may also experience cardiac, hepatic, renal, and central nervous system disease

Bacterial Superi nfection of COVID-19-Associated Pneumonia

- However, empiric broad-spectrum antimicrobial therapy is the standard of care for the treatment of shock
- Antibiotic stewardship is critical to avoid reflexive or continued courses of antibiotics

Inflammatory Response Due to COVID-19

- increased levels of pro-inflam. cytokines and anti-inflammatory cytokines,

"cytokine release syndrome" or "cytokine storm,"

- misnomers : the magnitude of cytokine elevation in patients with COVID-19 is modest compared to other critical illnesses(sepsis and ARDS)
- Patients with COVID-19 and severe pulmonary involvement : also manifest extrapulmonary disease and to exhibit laboratory markers of acute inflammation

And typically progress to critical illness 10 to 12 days after the onset of COVID-19 symptoms.

Multisystem Inflammatory Syndrome in Adults

- minimal respiratory symptoms
- laboratory markers of severe inflammation (elevated CRP, ferritin, D-dimer, cardiac enzymes, liver enzymes, and cr.)
- various other symptoms:fever and shock; and signs of cardiovascular, GI,dermatologic, and neurologic disease
- constellation of signs and symptoms has been designated **multisystem inflammatory syndrome in adults (MIS-A)**
- To date, most adults in whom MIS-A has been described have survived

Multisystem Inflammatory Syndrome in Adults

defined by the following criteria:

1. A severe illness requiring hospitalization in an individual aged ≥21 years
2. Current or past infection with SARS-CoV-2
3. Severe dysfunction in one or more extrapulmonary organ systems
4. Laboratory evidence of elevated inflammatory markers (CRP, ferritin, D-dimer, interleukin [IL]-6
5. Absence of severe respiratory illness
6. Absence of an alternative unifying diagnosi
7. one of exclusion after other causes (septic shock)

- case reports have described the use of intravenous immunoglobulin, corticosteroids, or anti-IL-6 therapy.

COVID-19-Induced Cardiac Dysfunction, Including Myocarditis

cardiac injury or dysfunction in approximately **20%** of hospitalized patients

1. **acute coronary syndrome**
2. **Myocarditis**
3. **arrythmias**
4. **thromboembolic disease**

Thromboembolic Events

- COVID-19 Critically ill patients : prothrombotic state
- characterized by :

  the elevation of certain biomarkers
- In some studies, thromboemboli have been diagnosed in patients who received chemical prophylaxis with heparinoids
- Autopsy studies provide : **thromboembolic disease** and **microvascular thrombosis**

major morbidity and mortality from (COVID-19) :

acute viral pneumonia (ARDS)

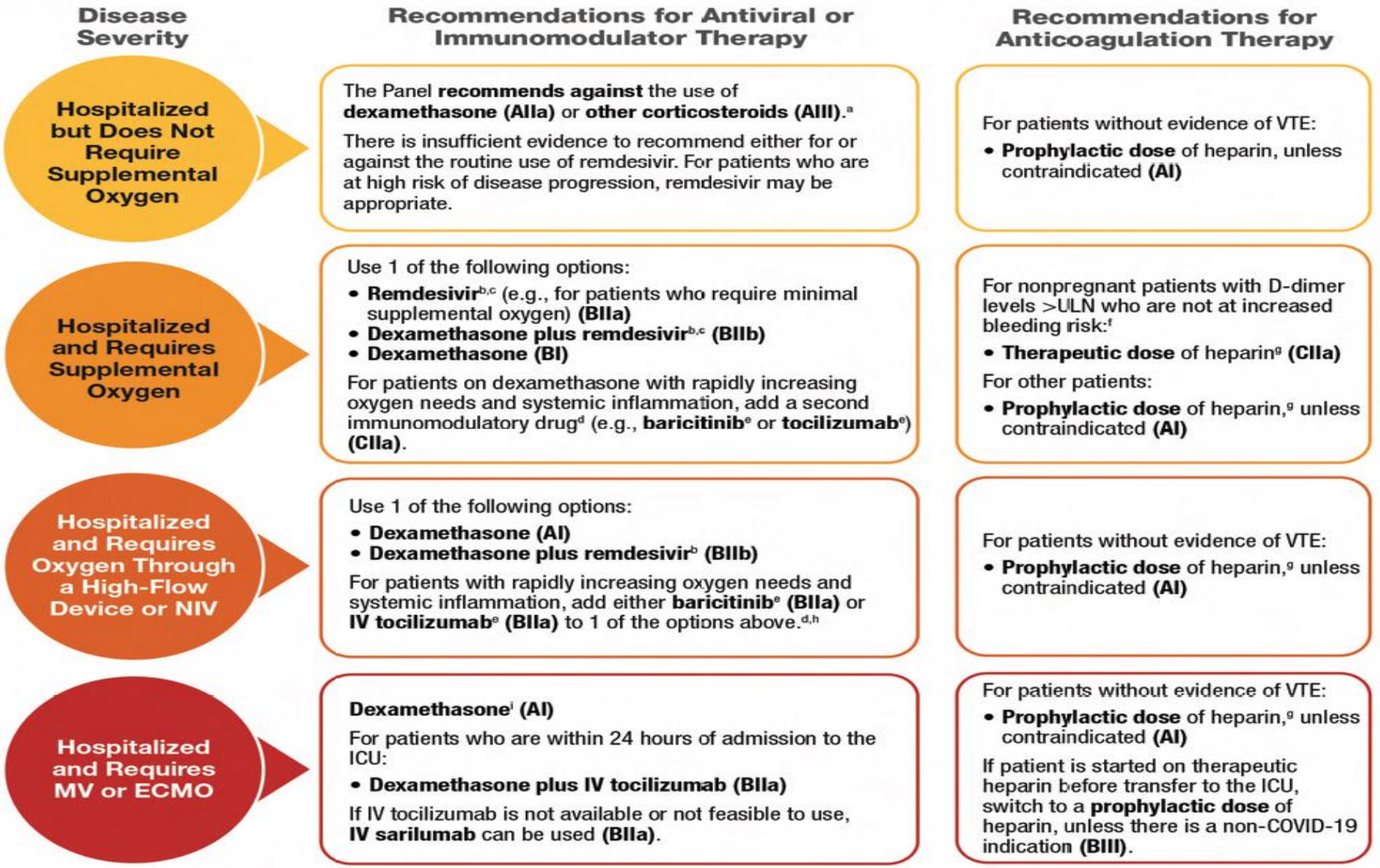
Progression leads to increasing respiratory support and intensive care unit level of care

Figure 1. Therapeutic Management of Nonhospitalized Adults With COVID-19

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Does Not Require Hospitalization or Supplemental Oxygen	All patients should be offered symptomatic management **(AIII)**. For patients who are at high risk of progressing to severe COVID-19,[a] use 1 of the following treatment options: **Preferred Therapies** *Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)[b,c] (AIIa)** • **Remdesivir[c,d] (BIIa)** **Alternative Therapies** *For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:* • **Bebtelovimab[e] (CIII)** • **Molnupiravir[c,f] (CIIa)** The Panel **recommends against** the use of **dexamethasone[g]** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.
Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone[g] (AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen[h]*	There is insufficient evidence to recommend either for or against the continued use of remdesivir or dexamethasone.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured[i]*	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not exceed** 10 days) with careful monitoring for AEs **(BIII)**. Since remdesivir is recommended for patients with similar oxygen needs who are hospitalized,[j] clinicians may consider using it in this setting. As remdesivir requires IV infusions for up to 5 consecutive days, there may be logistical constraints to administering remdesivir in the outpatient setting.

Rating of Recommendations: A = Strong; B = Moderate; C = Weak
Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Figure 2. Therapeutic Management of Adults Hospitalized for COVID-19 Based on Disease Severity



Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

an increase in risk for at least one severe COVID-19 outcome(CDC)

- Cancer
- Cerebrovascular disease
- Chronic kidney disease*
- Chronic lung diseases limited to:
  - Interstitial lung disease
  - Pulmonary embolism
  - Pulmonary hypertension
  - Bronchiectasis
  - COPD (chronic obstructive pulmonary disease)
- Chronic liver diseases limited to:
  - Cirrhosis
  - Non-alcoholic fatty liver disease
  - Alcoholic liver disease
  - Autoimmune hepatitis
- Cystic fibrosis
- Diabetes mellitus, type 1 and type 2*

- Disabilities
  - Attention-Deficit/Hyperactivity Disorder (ADHD)
  - Cerebral Palsy
  - Congenital Malformations (Birth Defects)
  - Limitations with self-care or activities of daily living
  - Intellectual and Developmental Disabilities
  - Learning Disabilities
  - Spinal Cord Injuries
  - (For the list of all conditions that were part of the review, see the module below)
- Heart conditions (such as heart failure, coronary artery disease, or cardiomyopathies)
- HIV (human immunodeficiency virus)
- Mental health disorders limited to:
  - Mood disorders, including depression
  - Schizophrenia spectrum disorders

- Neurologic conditions limited to dementia
- Obesity (BMI ≥30 kg/m^2)*
- Primary Immunodeficiencies
- Pregnancy and recent pregnancy
- Physical inactivity
- Smoking, current and former
- Solid organ or hematopoietic cell transplantation
- Tuberculosis
- Use of corticosteroids or other immunosuppressive medications

Suggestive higher risk for severe COVID-19 outcomes

The evidence is supported by mostly cohort, case-control, or cross-sectional studies.

- Children with certain underlying conditions
- Overweight (BMI ≥25 kg/m^2, but <30 kg/m^2)
- Sickle cell disease
- Substance use disorders
- Thalassemia

Mixed evidence

- Alpha 1 antitrypsin deficiency
- Asthma
- Bronchopulmonary dysplasia
- Hepatitis B
- Hepatitis C
- Hypertension

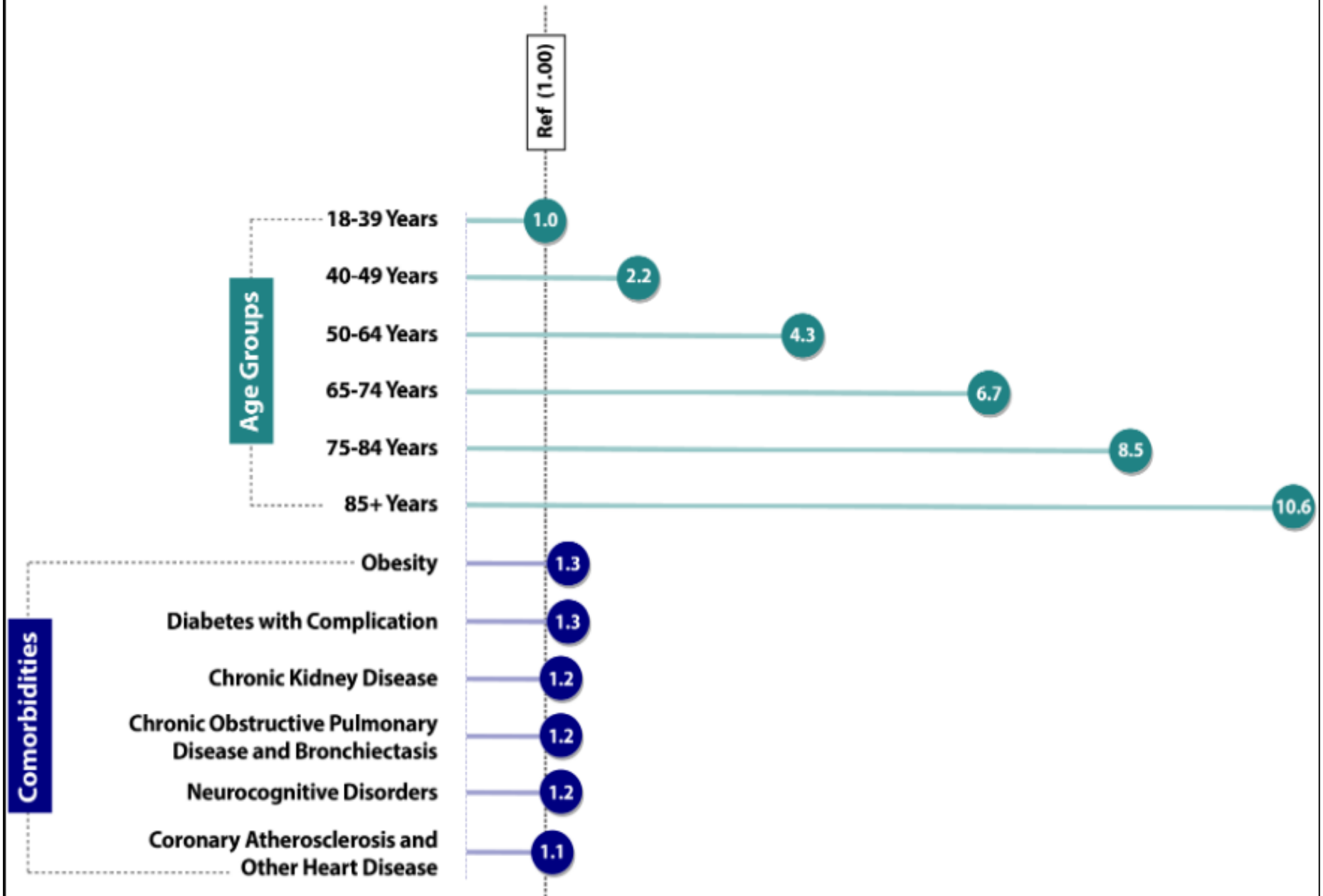
Underlying Medical Conditions and Severe Illness Among 540,667 Adults Hospitalized With COVID-19, March 2020–March 2021

- cross-sectional study
- The database included reports from 592 acute care hospitals in the US.
- The study was designed to examine risk factors associated with severe outcomes of COVID-19 including admission to an ICU or step down unit, invasive mechanical ventilation, and death.

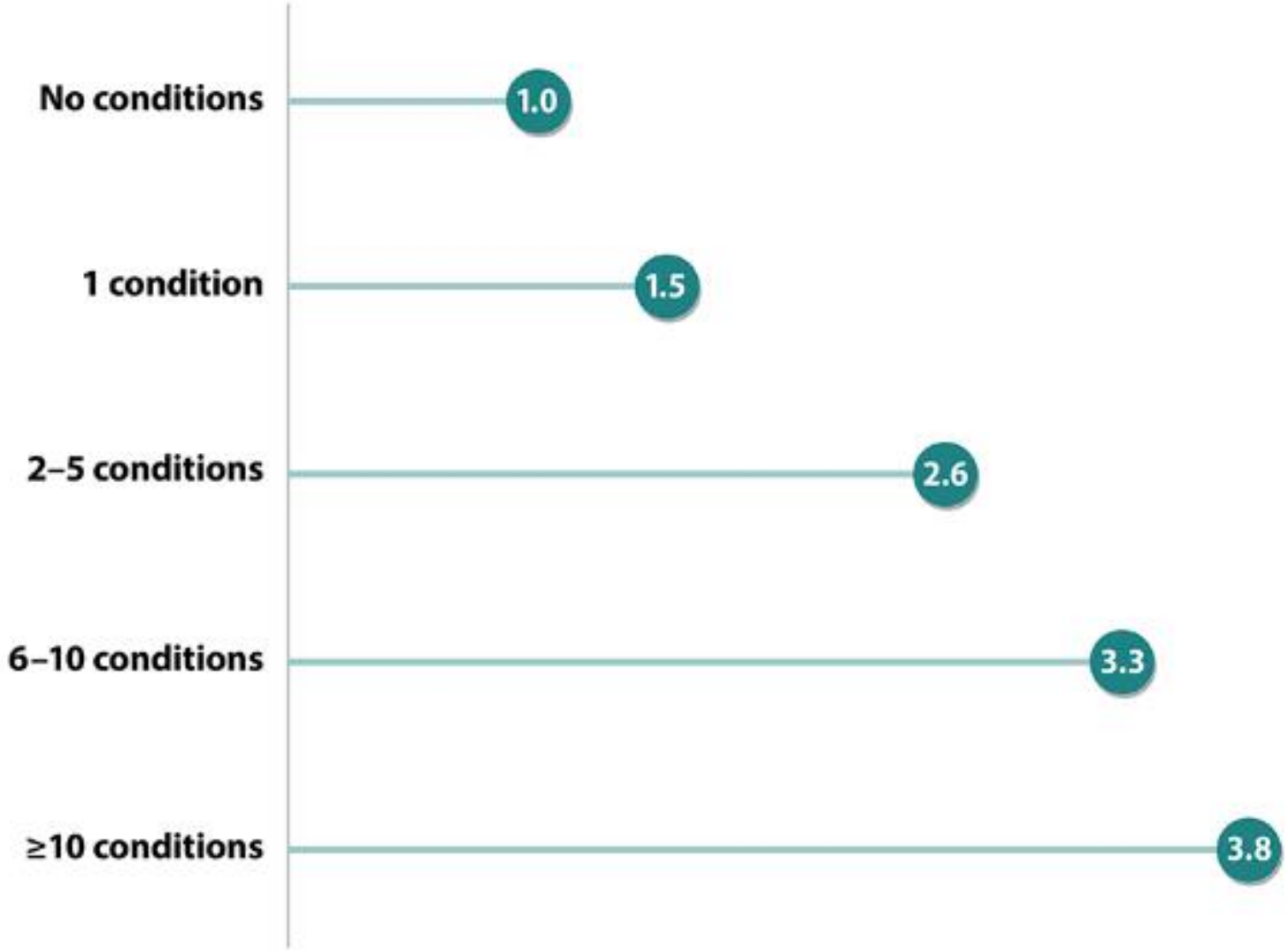
Main Findings:

- Certain underlying medical conditions increased risk for severe COVID-19 illness in adults.
- Having multiple conditions also increased risk.
- ***Obesity, diabetes with complications, and anxiety and fear-related disorders*** had the strongest association with death.
- The risk associated with a condition ***increased with age.***

COVID-19 Death Risk Ratio (RR) for Select Age Groups and Comorbid Conditions



COVID-19 Death Risk Ratio (RR) Increases as the Number of Comorbid Conditions Increases

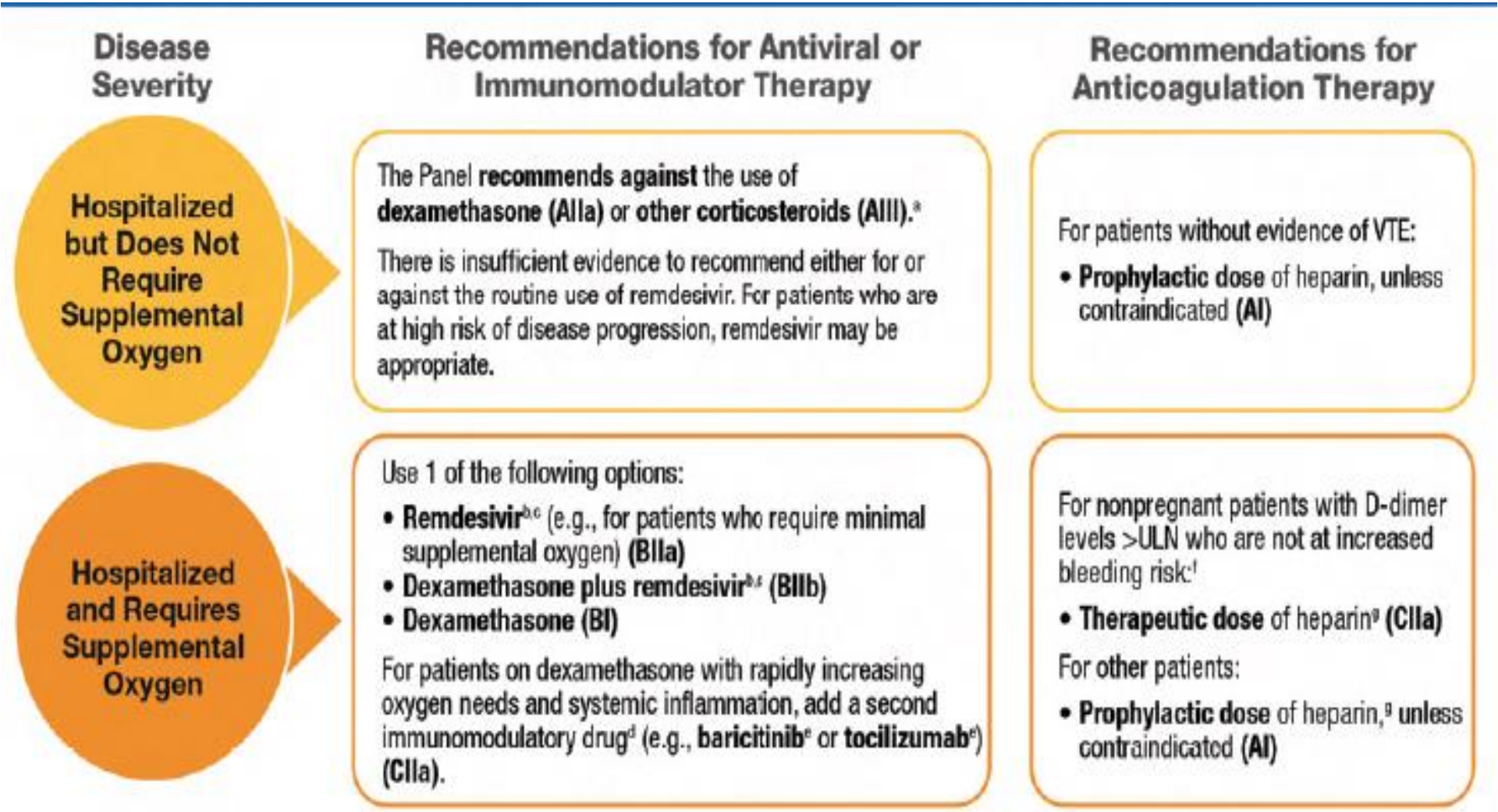


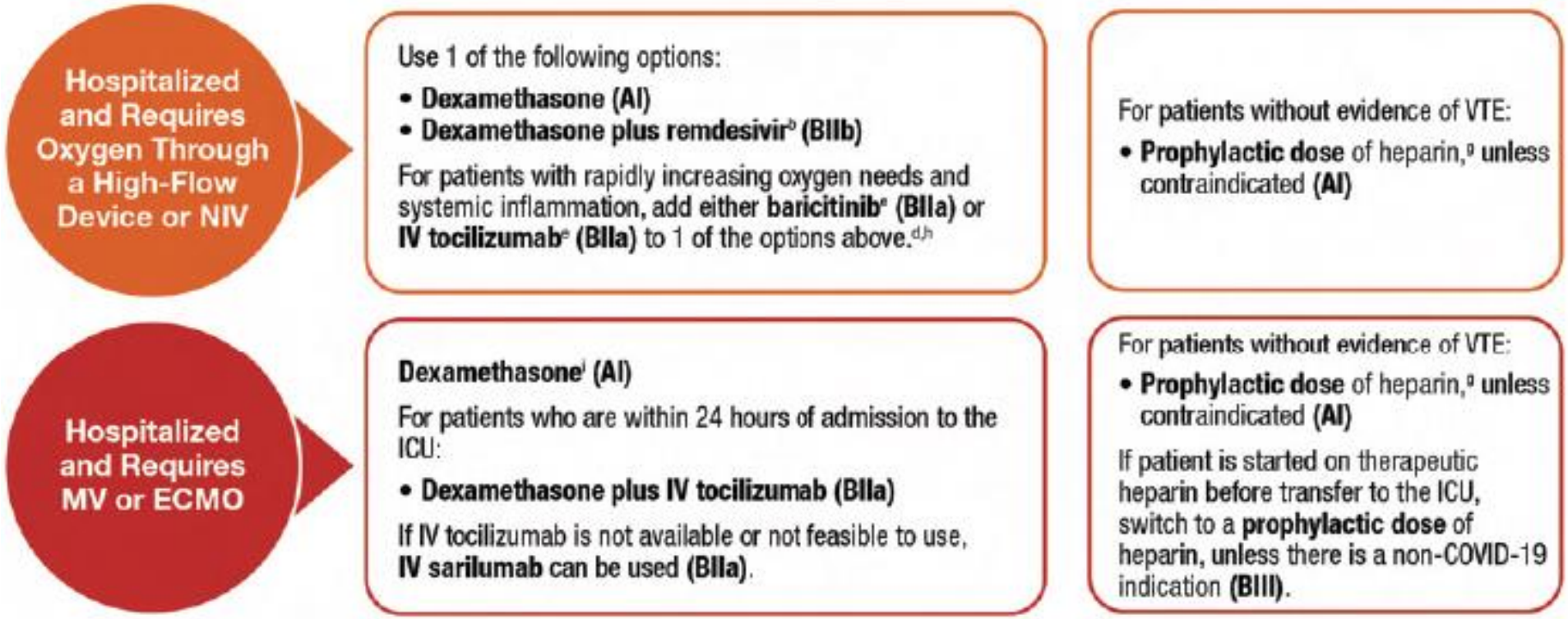
Therapeutic Management of Nonhospitalized Adults With COVID-19

PATIENT DISPOSITION	PANEL'S RECOMMENDATIONS
Does Not Require Hospitalization or Supplemental Oxygen	All patients should be offered symptomatic management **(AIII)**. For patients who are at high risk of progressing to severe COVID-19,[a] use 1 of the following treatment options: **Preferred Therapies** *Listed in order of preference:* • **Ritonavir-boosted nirmatrelvir (Paxlovid)[b,c] (AIIa)** • **Remdesivir[c,d] (BIIa)** **Alternative Therapies** *For use ONLY when neither of the preferred therapies are available, feasible to use, or clinically appropriate. Listed in alphabetical order:* • **Bebtelovimab[e] (CIII)** • **Molnupiravir[c,f] (CIIa)** The Panel **recommends against** the use of **dexamethasone[g]** or **other systemic corticosteroids** in the absence of another indication **(AIII)**.

Discharged From Hospital Inpatient Setting in Stable Condition and Does Not Require Supplemental Oxygen	The Panel **recommends against** continuing the use of **remdesivir (AIIa)**, **dexamethasone**[g] **(AIIa)**, or **baricitinib (AIIa)** after hospital discharge.
Discharged From Hospital Inpatient Setting and Requires Supplemental Oxygen *For those who are stable enough for discharge but who still require oxygen*[h]	There is insufficient evidence to recommend either for or against the continued use of remdesivir or dexamethasone.
Discharged From ED Despite New or Increasing Need for Supplemental Oxygen *When hospital resources are limited, inpatient admission is not possible, and close follow-up is ensured*[i]	The Panel recommends using **dexamethasone** 6 mg PO once daily for the duration of supplemental oxygen (dexamethasone use **should not exceed** 10 days) with careful monitoring for AEs **(BIII)**. Since remdesivir is recommended for patients with similar oxygen needs who are hospitalized,[j] clinicians may consider using it in this setting. As remdesivir requires IV infusions for up to 5 consecutive days, there may be logistical constraints to administering remdesivir in the outpatient setting.

Therapeutic Management of Hospitalized Adults With COVID-19




Hospitalized and Requires Oxygen Through a High-Flow Device or NIV
Use 1 of the following options:
• Dexamethasone (AI)
• Dexamethasone plus remdesivir[b] (BIIb)
For patients with rapidly increasing oxygen needs and systemic inflammation, add either baricitinib[e] (BIIa) or IV tocilizumab[e] (BIIa) to 1 of the options above.[d,h]
For patients without evidence of VTE:
• Prophylactic dose of heparin,[g] unless contraindicated (AI)
Hospitalized and Requires MV or ECMO
Dexamethasone[i] (AI)
For patients who are within 24 hours of admission to the ICU:
• Dexamethasone plus IV tocilizumab (BIIa)
If IV tocilizumab is not available or not feasible to use, IV sarilumab can be used (BIIa).
For patients without evidence of VTE:
• Prophylactic dose of heparin,[g] unless contraindicated (AI)
If patient is started on therapeutic heparin before transfer to the ICU, switch to a prophylactic dose of heparin, unless there is a non-COVID-19 indication (BIII).

Respiratory support:

1-oxygenation with low-flow and high-flow systems
2- noninvasive ventilation
3- the use of other adjunctive therapies (nebulized medications) and rescue therapies (prone positioning)

some patients improve and respiratory support can be de-escalated, a proportion continue to deteriorate:

4- intubation and mechanical ventilation.

Prone position

hospitalized patients with hypoxemic respiratory failure on:

1-low-flow oxygen
2-HFNC
3-NIV

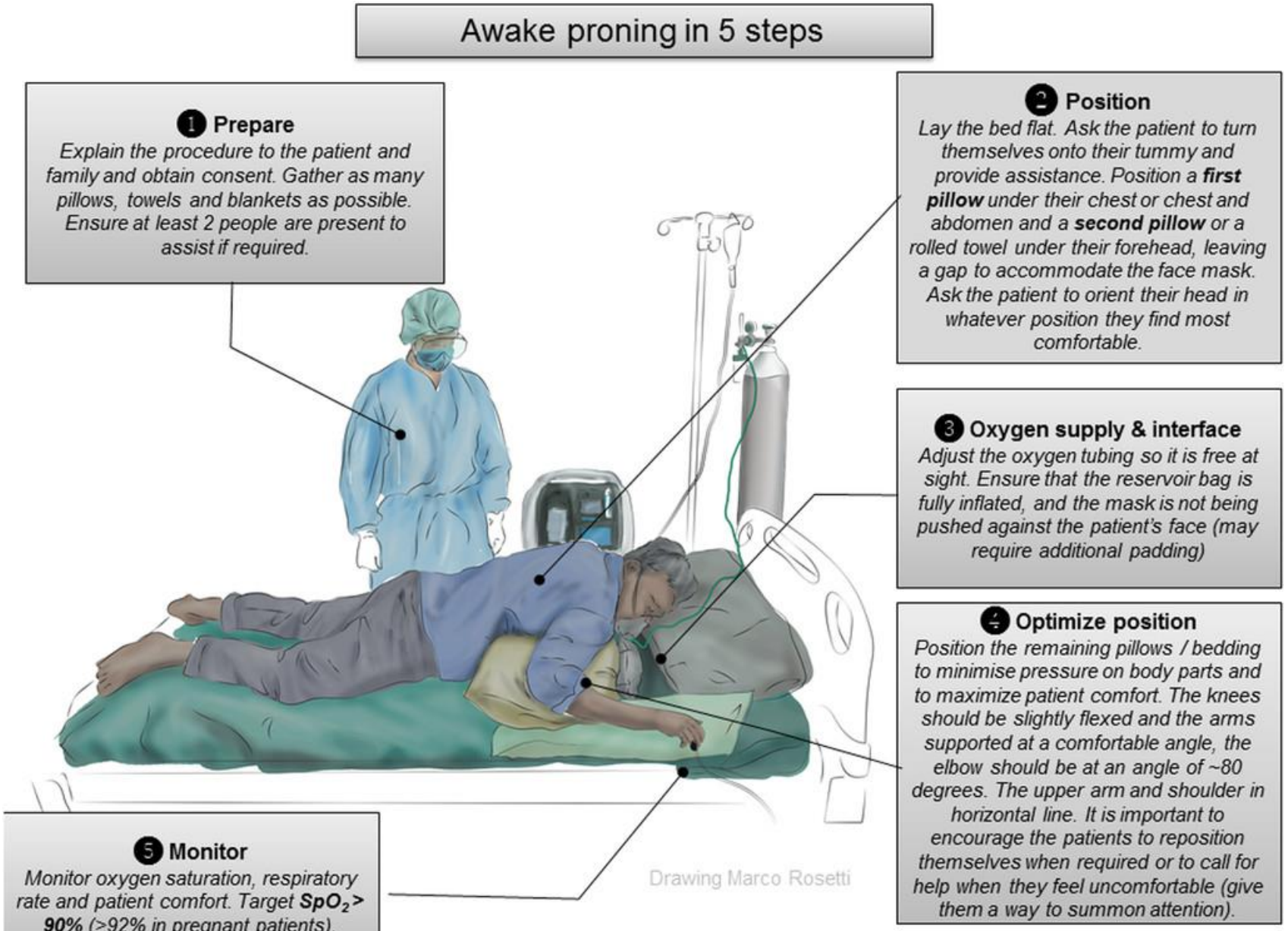
at least 6 to 8 hours prone in a 24-hour period

Prone position

limited direct evidence:

1-transient improvement in oxygenation
2- possible reduction in intubation rates
3- efficacy in ventilated patients with ARDS
4-not to reduce mortality

Figure 2.



Visual aid to facilitate awake proning implementation in a resource-limited setting. Suggested position is an indication and could be adapted based on patient preferences. Adapted with permission from a prone positioning checklist developed by Dr. Rebecca Inglis in Lao PDR.67

Prone position: Contraindications

Contraindications
Acute bleeding (eg, hemorrhagic shock, massive hemoptysis)
Multiple fractures or trauma (eg, unstable fractures of femur, pelvis, face)
Spinal instability
Raised intracranial pressure >30 mmHg or cerebral perfusion pressure <60 mmHg
Tracheal surgery or sternotomy within two weeks

Relative contraindications
Shock (eg, persistent mean arterial pressure <65 mmHg)
Anterior chest tube(s) with air leaks*
Major abdominal surgery
Recent pacemaker*
Clinical conditions limiting life expectancy* (eg, oxygen or ventilator-dependent respiratory failure)
Severe burns*
Recent lung transplant recipient*

Prone position: complications

Complications
Nerve compression (eg, brachial plexus injury)
Crush injury
Venous stasis (eg, facial edema)
Dislodging endotracheal tube
Diaphragm limitation
Pressure sores (eg, facial)
Dislodging vascular catheters or drainage tubes
Retinal damage
Transient reduction in arterial oxygen saturation
Vomiting
Transient arrhythmias

Oxygenation targets

The World Health Organization suggests:

- titrating oxygen to a target peripheral oxygen saturation (SpO_2) of ≥94 percent during initial resuscitation
- ≥90 percent for maintenance oxygenation
- Hyperoxia should be avoided

- Individualization :important,
- lower target (eg, patients with a concomitant acute hypercapnic respiratory failure [COPD])
- higher target (eg, pregnancy)

PATIENTS WITH MINIMAL OXYGEN NEEDS

Low-flow oxygen

- up to 6 L/min. via nasal cannulae :

appropriate as an initial strategy

- The degree of viral aerosolization at low-flow rates is minimal.
- As flow increases: the risk may increase
- So : wear a droplet mask, especially during transport or when staff are in the room

PATIENTS WITH REQUIREMENTS FOR ADVANCED RESPIRATORY SUPPORT

- oxygen requirements **over 6 to 15 L/min** or breathing becomes labored

1-high-flow oxygen via nasal cannulae (HFNC)
2-noninvasive ventilation (NIV) device

concomitant **acute hypercapnia** or **heart failure** requiring bilevel or continuous positive airway pressure

Noninvasive modalities

- improve oxygenation and dyspnea
- preventing progression to intubation :

limitations

- higher intubation thresholds during the pandemic
- some may not proceed to intubation

Choosing oxygen via HFNC versus NIV

patient's comorbidities and the tolerability of the device

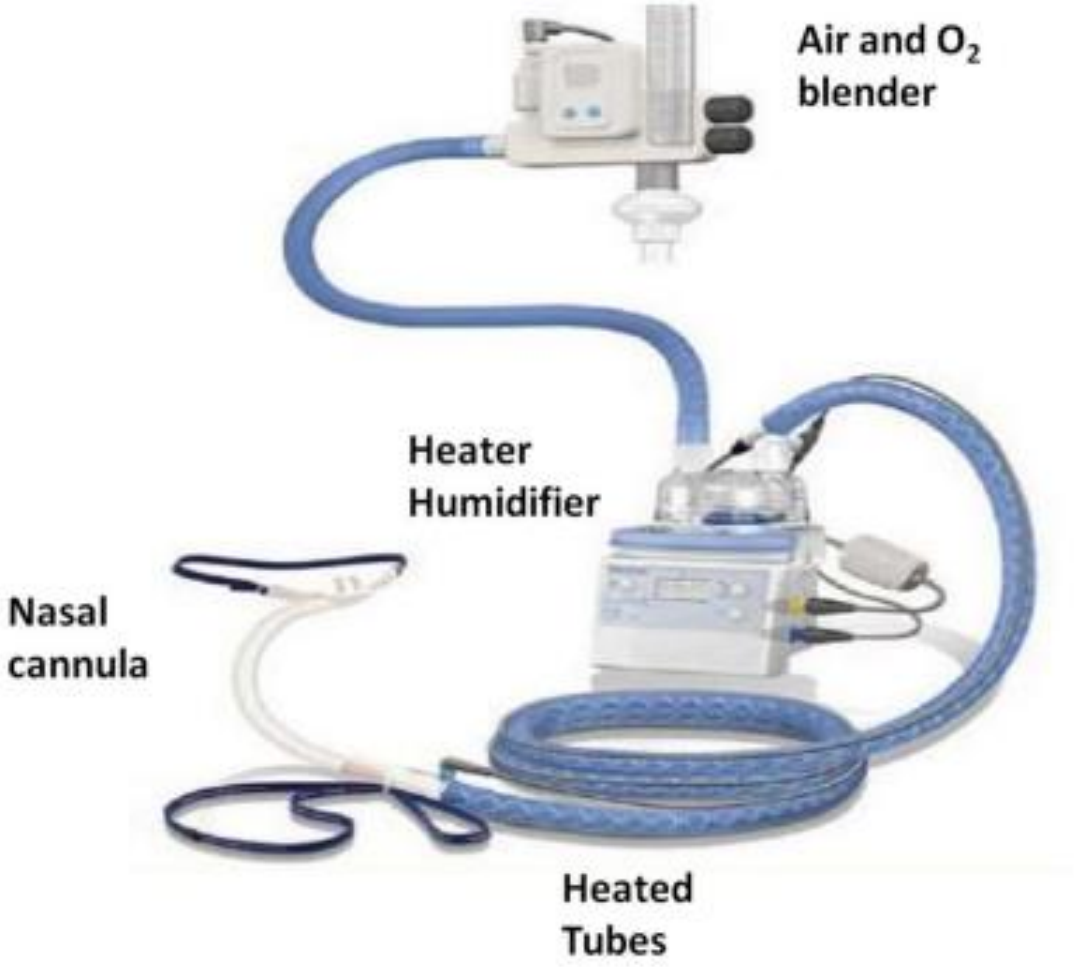
NIV :

1-AE of COPD
2-acute cardiogenic pulmonary edema
3-underlying sleep-disordered breathing
4-respiratory muscle weakness

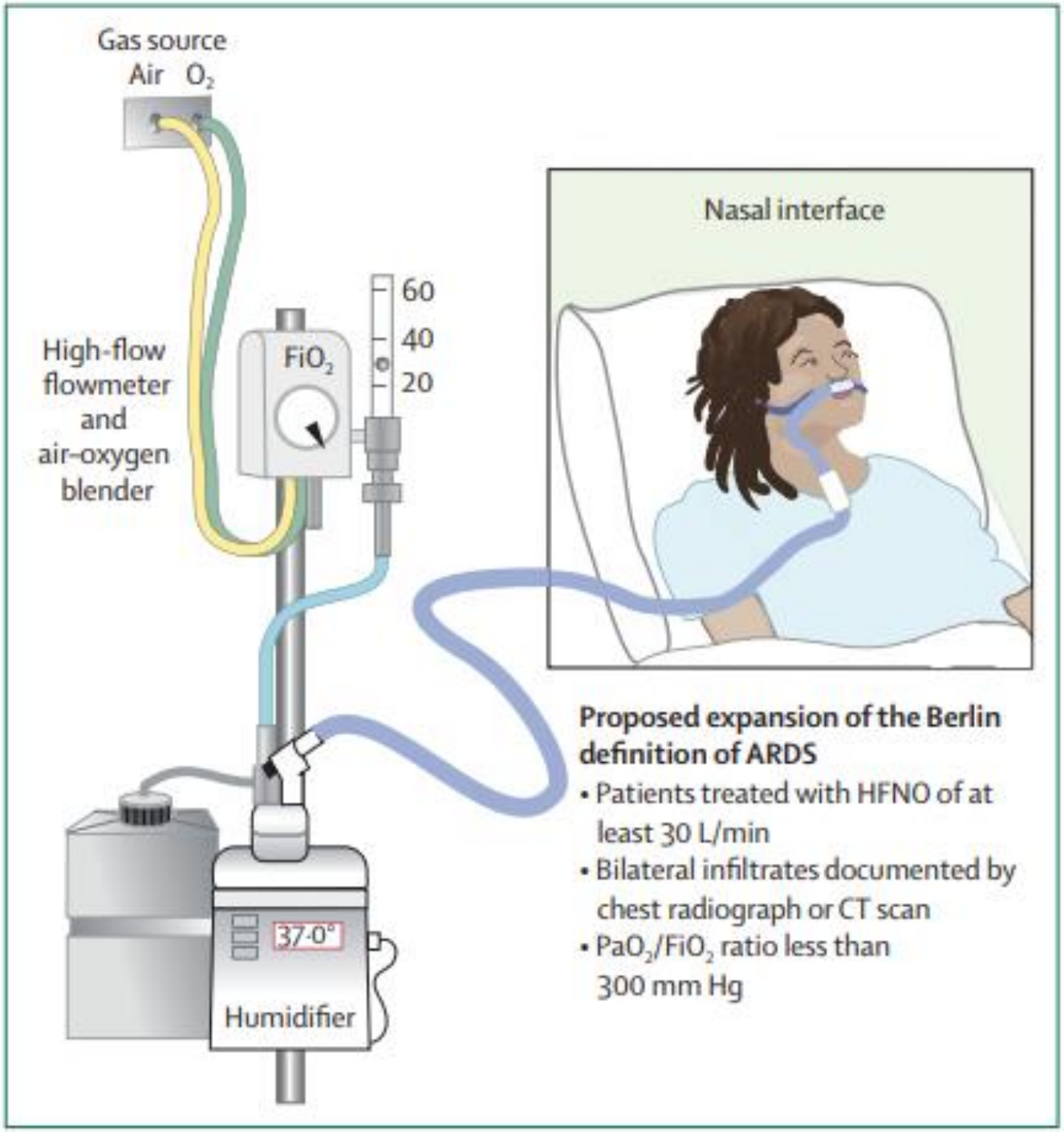
In the absence of such comorbidities, either modality is acceptable

HFNC:

1- fewer adverse events
2-more comfortable and practical mode
3-continue to converse and eat



Optiflow nasal high-flow system . The air–oxygen blender allows a fraction of inspired oxygen from 21% to 100% and generates a flow of up to 60l/min. The gas is heated and humidified through an active heated humidifier and delivered through a heated tube.



Proposed expansion of the Berlin definition of ARDS

- Patients treated with HFNO of at least 30 L/min
- Bilateral infiltrates documented by chest radiograph or CT scan
- PaO_2/FiO_2 ratio less than 300 mm Hg

NIV: Interface (mask)

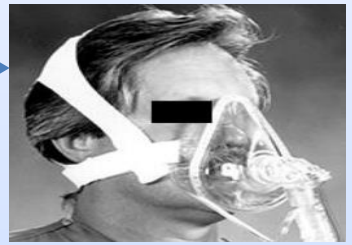
1-Oronasal mask

2-Nasal mask

3-Nasal prongs

4-Full face mask

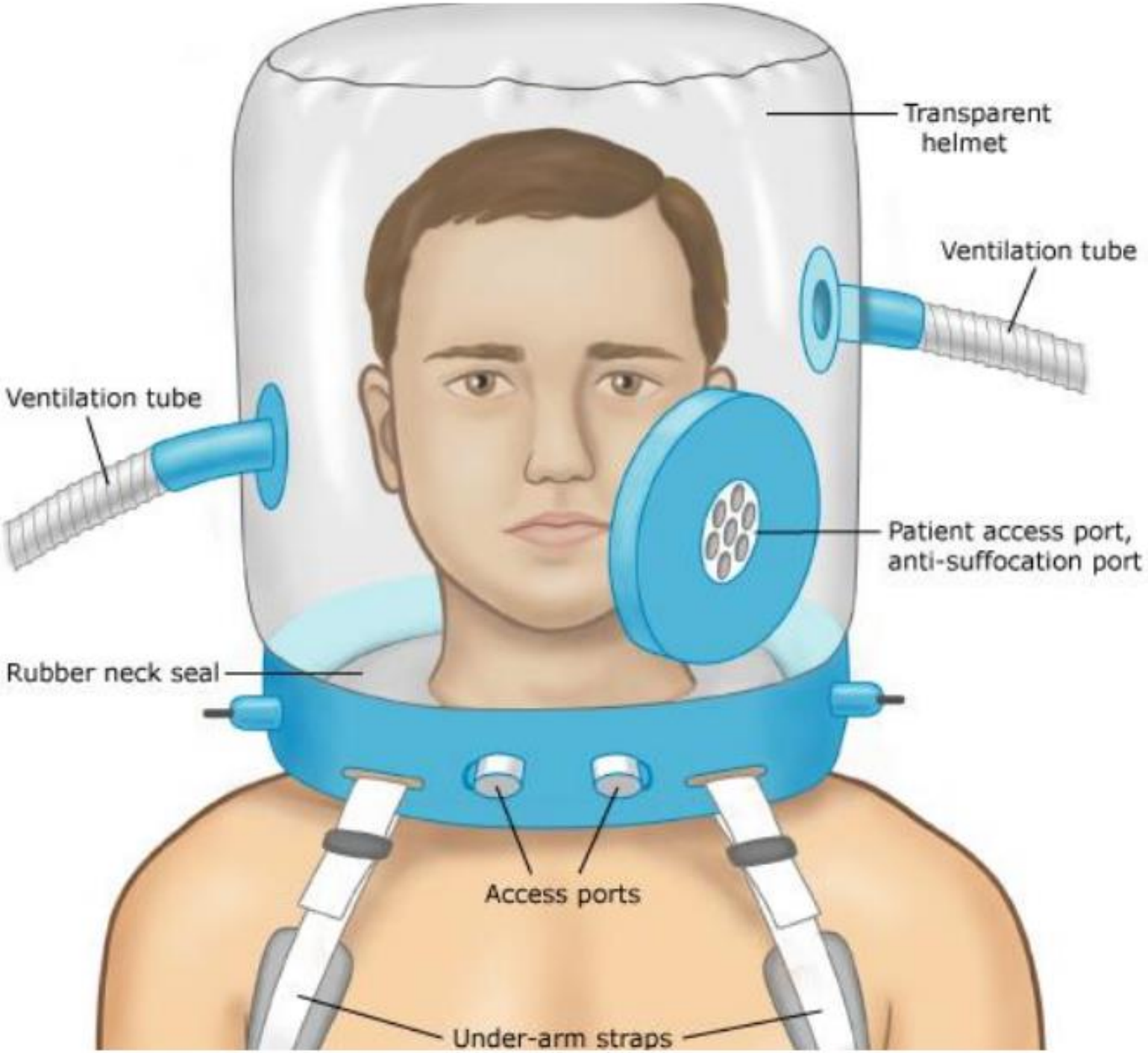
5-Mouth piece



NIV: Interface (mask)

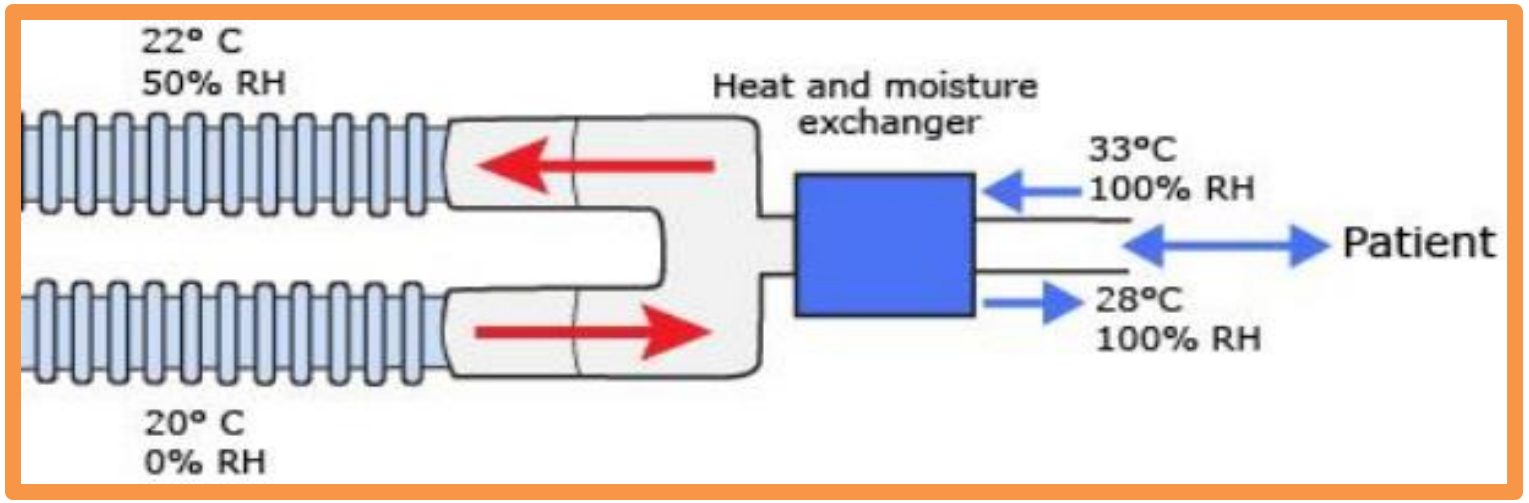
6-Helmet

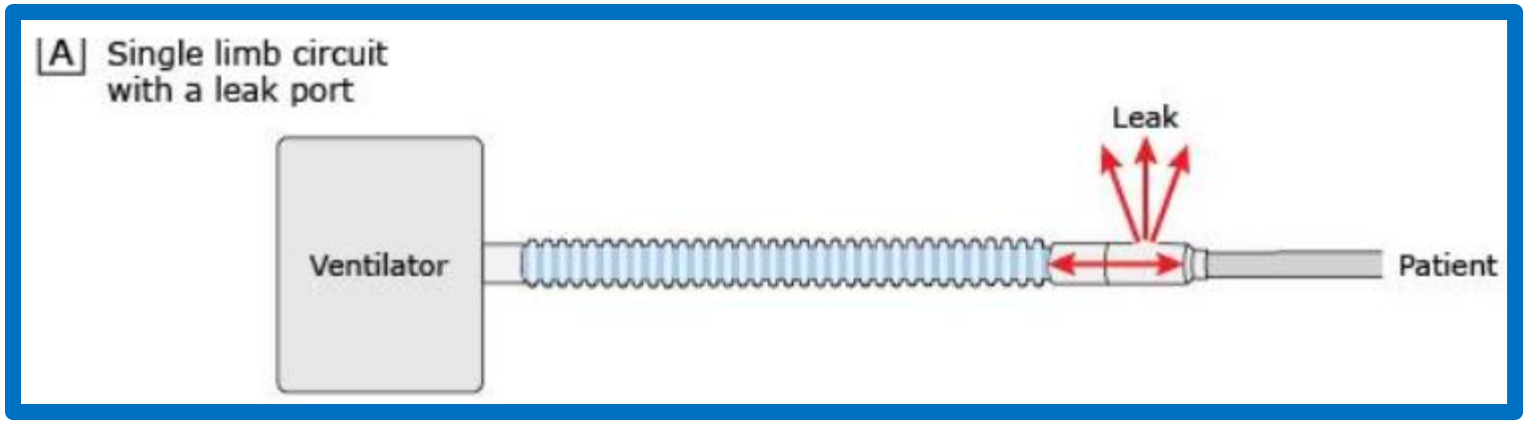
- talk, read, and drink through a straw
- minimizing complications such as skin necrosis, gastric distension, and eye irritation
- as a reservoir
- High flow and short inspiratory time are required to pressurize the helmet rapidly
- accumulation of CO_2
- noise exposure:hearing damage,
- more patient-ventilator asynchrony (due to delayed triggering and cycling), and less relief of inspiratory effort
- the actual tidal :unknown(distensibility of the device)
- droplet precautions COVID-19):unproven
- may reduce the risk of death and intubation : more suitable in PEEP-responsives


Transparent helmet
Ventilation tube
Ventilation tube
Patient access port, anti-suffocation port
Rubber neck seal
Access ports
Under-arm straps

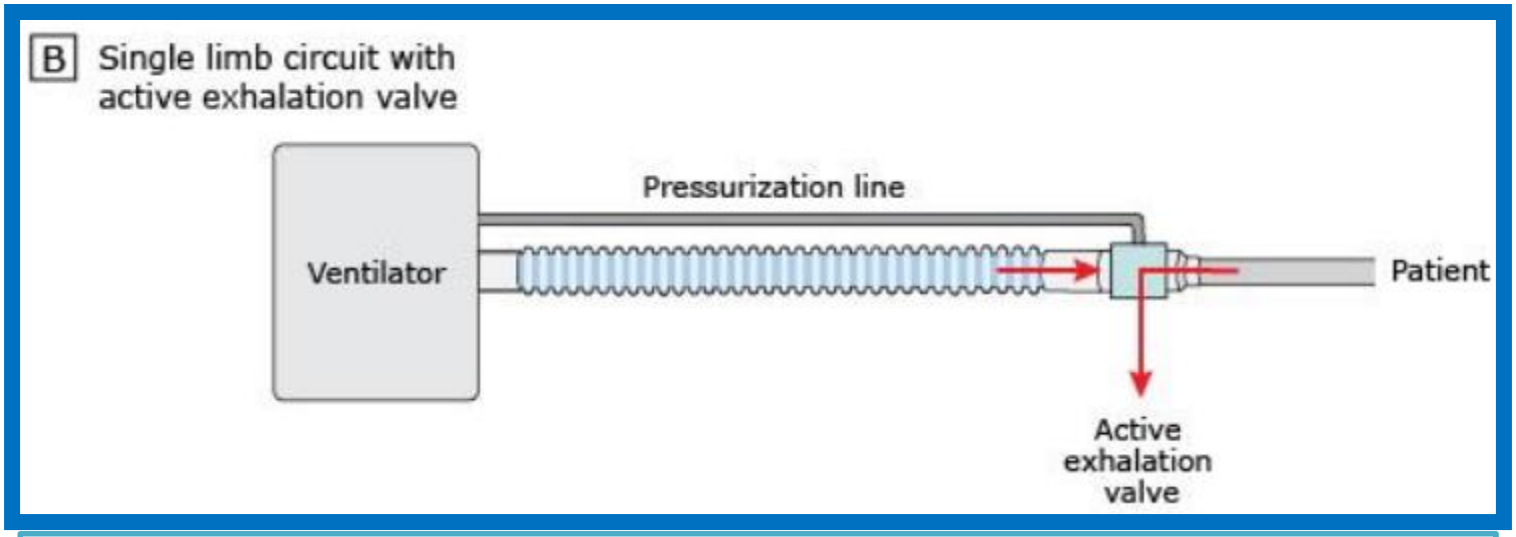
Ventilator circuit

- Positive pressure and oxygen are delivered
- standard mechanical ventilator :high flows up to an FiO_2 of 1
- many portable ventilators :lower flow (up to 10 or 15 liters of oxygen/minute, higher flows : helmet interface)
- Oxygen should be heated and humidified to improve tolerance and prevent mucosal
- For standard ventilators, typical dual-limb circuitry is used (with inspiratory and expiratory tubing) while portable ventilators typically have a single-limb circuit

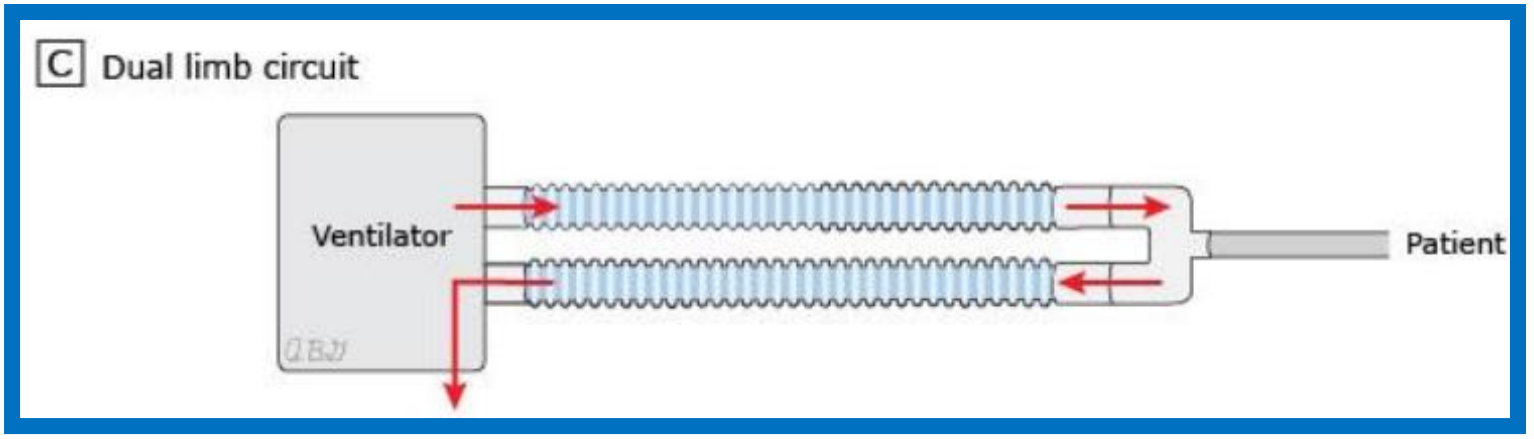




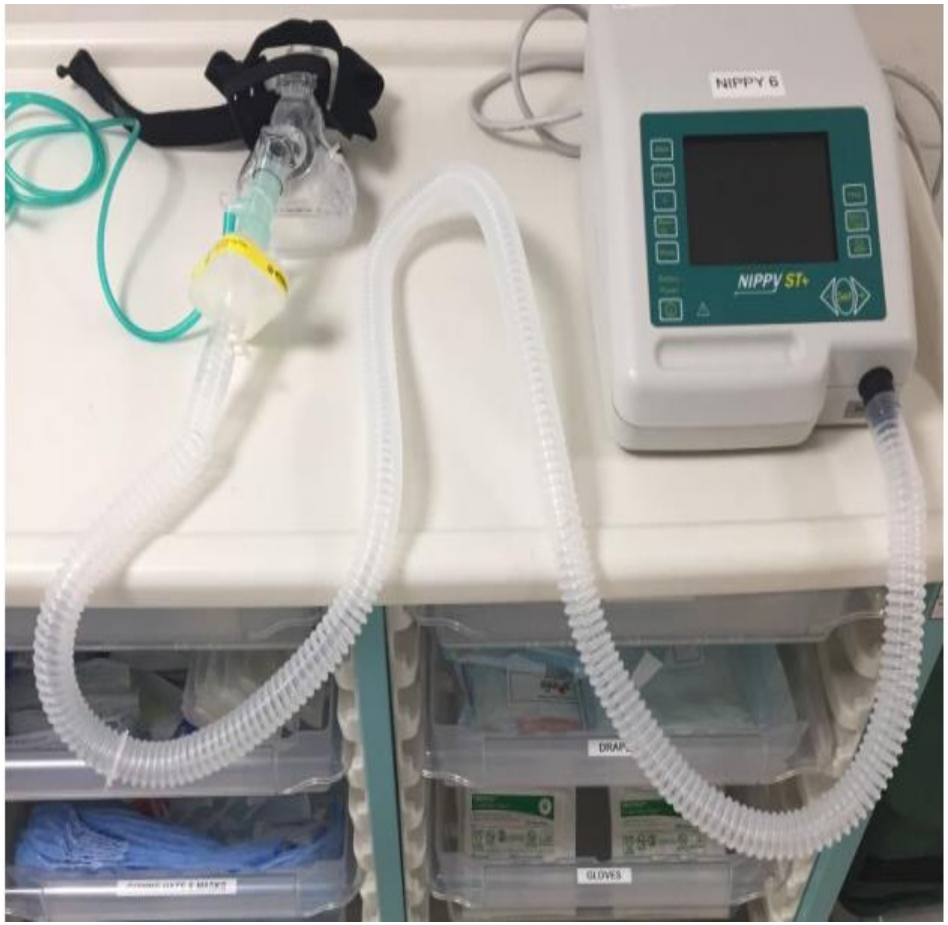
- the leak port is always open to atmosphere
- commonly used for noninvasive ventilation
- typical design for PAP devices for OSA

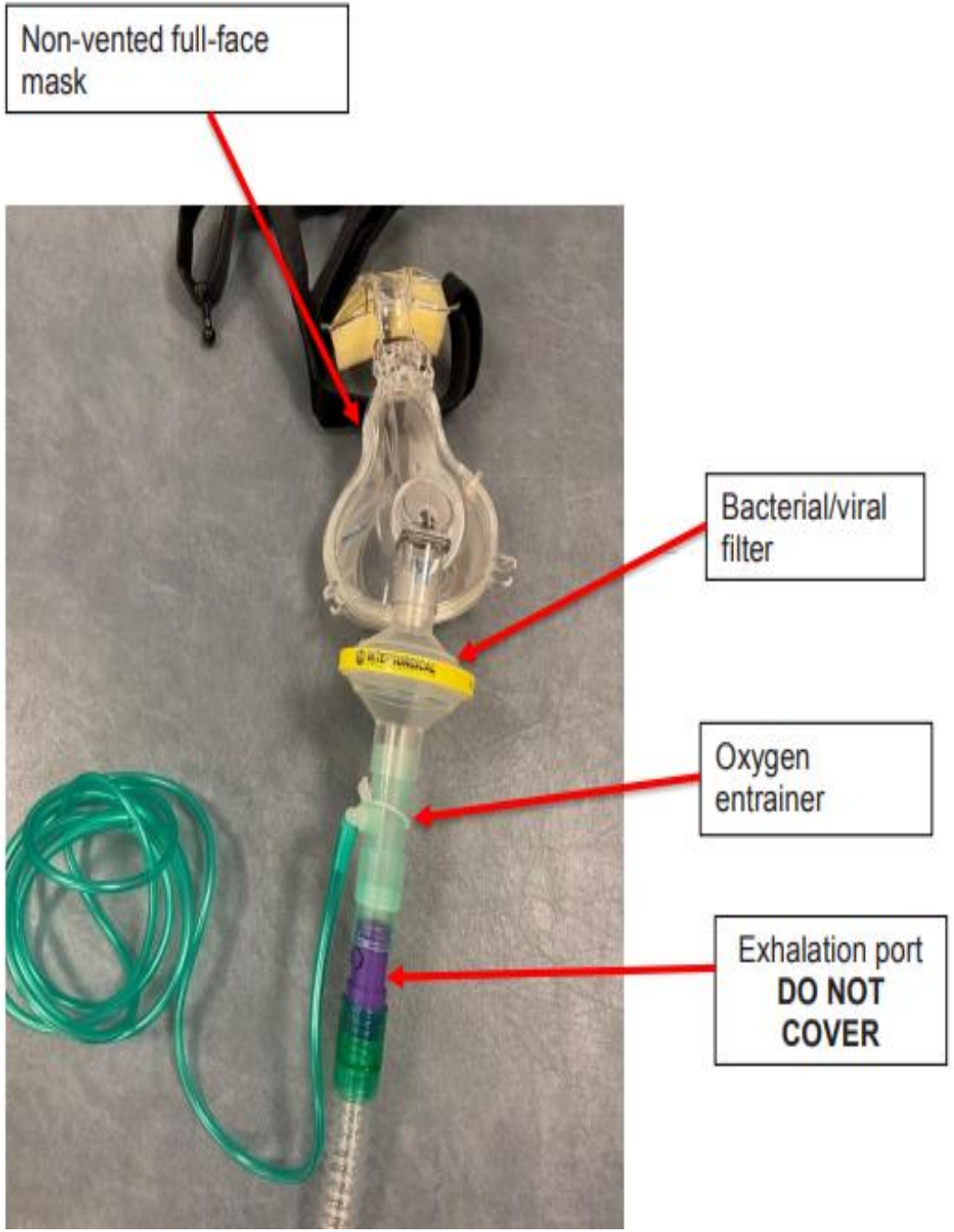


- typically : portable ventilators
- During inspiration, the exhalation valve is closed



- critical care ventilators
- the valves are within the ventilator.


NIPPY 6
NIPPY ST+
DRAP
GLOVES


Non-vented full-face mask
Bacterial/viral filter
Oxygen entrainer
Exhalation port
DO NOT COVER

INITIAL SETTINGS

Bilevel NIV (BPAP)

1- helpful in acute hypercapnic RF(AECOPD)

2-acute hypoventilation:

- drug overdose
- neuromuscular disorders
- OHS

3-nonhypercapnic hypoxemic acute RF:

- pneumonia
- early ARDS
- asthma

CPAP:

acute cardiogenic pulmonary edema but bilevel NIV : appropriate alternative especially when hypercapnia is present or if CPAP fails.

Protocol for initiation of noninvasive ventilation

Initiation

- Appropriately monitored location, oximetry, respiratory impedance, vital signs as clinically indicated
- Patient in bed or chair at >30-degree angle
- Select and fit interface
- Select ventilator
- Apply headgear; avoid excessive strap tension (one or two fingers under strap)
- Connect interface to ventilator tubing and turn on ventilator

Initial settings

Bilevel NIV	CPAP	PSV
➢ Start with low pressure with backup rate: IP at 8 to 12 cm H_2O; EP at 3 - 5 cm H_2O ➢ Gradually increase IP(10 - 20 cm H_2O) as tolerated to achieve alleviation of dyspnea, decreased RR, increased TV ➢ O_2 to keep SPO_2 >90%	➢ CPAP level at 5 to 8 cm H_2O ➢ Gradually increase as tolerated (up to 20 cm H_2O): improvement in dyspnea and reduction in RR ➢ Provide O_2 to keep SPO2>90%	➢ IP at 8 to 12 cm H_2O ➢ PEEP at 3 to 5 cm H_2O ➢ Gradually increase IP to max. of 20 cm H_2O to achieve improvement in dyspnea and reduction in RR

Follow-up

- Check for air leaks, readjust straps as needed
- Add humidifier as indicated
- Consider mild sedation (eg, intravenously administered lorazepam 0.5 mg) in agitated patients
- Encouragement, reassurance, and frequent checks and adjustments as needed
- Monitor occasional blood gases (within 1 to 2 hours) and then as needed

Bilevel noninvasive ventilation

- IPAP minus EPAP ("delta" PAP) determines TV
- **the spontaneous/timed (S/T) setting with a backup rate of 8 to 12**

  rarely timed mode (only supported during timed breaths)
- **IPAP 8 to 12 cm H_2O**
  - ✓ increments of 2 cm H_2O, to a maximum of 20 cm H_2O
  - ✓ titration for improved dyspnea, decreased RR, increased TV and VE, and good patient-ventilator synchrony
  - ✓ adequate TV treating acute hypercapnia.
- **EPAP 3 to 5 cm H_2O**
  - ✓ If oxygenation remains inadequate, the EPAP may also be increased minimally (up to 10 cm H_2O)
  - ✓ may decrease the delivered TV
- **FiO_2 to keep SpO_2 >90 percent** target :underlying disorder

CPAP

- continuous level of PAP throughout the respiratory cycle
- patients must initiate all breaths
- spontaneous TV is augmented with CPAP, the TV cannot be titrated as effectively as bilevel NIV
- not the optimal mode for treating disorders that require increased alveolar ventilation (disorders associated with acute hypercapnia)
- However, since CPAP is functionally similar to PEEP: more effective at improving oxygenation than ventilation
- initial settings:
  - Mode: CPAP
  - CPAP level: 5 to 8 cm H_2O
  - FiO_2: SpO_2 >90 percent
- titrated up to 20 cm H_2O : improvement of dyspnea and decreased RR
- up to 25 cm H_2O : generally poorly tolerated

Trial success

- successful trial : both clinical and gas exchange criteria are improved
- persisting with NIV and monitoring for another two hours or more for continued success is reasonable
- Monitoring for complications such as aspiration and pressure ulcers
- Continued improvement : weaning
- deterioration : intubation and MV

Trial failure

- no improvement, or deterioration (1-2 hr.):

  promptly intubated

- Clinical criteria suggesting failure :

  1- worsening gas exchange
  2-increasing RR
  3-worsening encephalopathy or agitation
  4- inability to clear secretions
  5- inability to tolerate any of the interfaces
  6-hemodynamic instability

- failure rates are high : approximately ***one-third*** of patients (relate to the underlying disorder)

Weaning

- gas exchange and clinical parameters of acute respiratory failure have improved dramatically and the cause of respiratory failure has improved:

1.RR ≥12 and ≤22 /minute
2.SpO_2 ≥90 percent on ≤60 percent FiO_2 or predicted needs can be met with oxygen delivered via HFNC or low flow oxygen
3.Hemodynamic stability (off or on low dose vasopressors and HR ≥50 and ≤120 /min.)
4.pH >7.25
5.patient should ideally be afebrile, awake and alert, or easily arousable
6.Minimal NIV settings (bilevel PAP 10 cm H_2O/5 cm H_2O or CPAP ≤10 cm H_2O).

- progressively decreasing the amount of PAP, or by permitting the patient to be disconnected from the NIV for progressively longer durations, or a combination of both

Management of the intubated adult

Diagnostic testing	Actions	Explanatory notes
NP swab	➢ **Perform SARS-CoV-2 (COVID-19) test** ➢ **Test for influenza if prevalent in the community** ➢ **Do NOT obtain viral cultures**	➢ In intubated patients, **tracheal aspirates** and nonbronchoscopic alveolar lavage **("mini-BAL")** are also acceptable. ➢ **Bronchoscopy** is only performed for this indication when upper respiratory samples and mini-BAL are negative.

Diagnostic testing	Actions	Explanatory notes
Baseline lab. testing	Obtain the following: ➢ CBC with differential counts ➢ Urinalysis ➢ Chemistry panel including LFTs ➢ Troponin and BNP at baseline, and subsequently as indicated ➢ Consider biomarkers at baseline and for interval monitoring if indicated: procalcitonin, ferritin, CRP, CPK, D-dimer, triglycerides, fibrinogen, LDH	➢ lymphopenia is common, resulting in a high ratio (>50) of neutrophils:lymphocytes ➢ Elevated LFTs:common ➢ Procalcitonin : often low early in illness. ➢ ***Lymphopenia and elevation of LDH, ferritin, and CRP*** **: disease progression and need for MV**
Other microbiology	➢ Blood cultures, if clinically indicated ➢ Sputum culture, if clinically indicated (avoid induced sputum) ➢ Urinary antigen for *Legionella*, *Pneumococcus*, if clinically indicated	

Diagnostic testing	Actions	Explanatory notes
Imaging	➢ Obtain **portable chest radiograph** ➢ **POC ultrasound** may provide additional information ➢ **CT only** in patients with an indication that would change management	➢ Main role of **POC ultrasound** is to identify other causes of respiratory compromise (eg, pneumothorax, pleural effusion, pericardial effusion, heart failure) or other contributors to hypotensive shock. ➢ Characteristic findings on POC ultrasound in COVID-19 pneumonia are nonspecific and include pleural thickening and B lines.

Diagnostic testing	Actions	Explanatory notes
ECG	➢ Baseline at admission ➢ Subsequent ECGs for patients on medications that can prolong QTc or patients with troponin elevation	➢ Medications that can prolong QTc include (among others): **azithromycin, hydroxychloroquine, remdesivir, phenothiazines, quetiapine**
FOB	➢ Avoid bronchoscopy to prevent aerosol spread unless indicated for reasons other than diagnosis ➢ If necessary, perform in airborne infection isolation room	➢ Bronchoscopy, should only be performed for the diagnosis of COVID-19 when upper respiratory samples and mini-BAL are negative or when indicated for another reason (eg, infection in an immunosuppressed patient; life-threatening hemoptysis or

Supportive care	Actions	Explanatory notes
➢ Management is largely supportive with surveillance for common complications including ***ARDS, acute kidney injury, elevated liver enzymes, and cardiac injury*** ➢ All co-infections and comorbidities should be managed ➢ Patients should be monitored for prolonged QTc interval and drug interactions.		

Supportive care	Actions	Explanatory notes
Vascular access	➢ Place central venous catheter if indicated (eg, ventilated patient) ➢ Place arterial line if frequent need for ABGs anticipated (eg, ventilated patient with ARDS) or blood pressure monitoring is needed ➢ Bundle procedures to minimize exposure; review procedure checklist before entering room	
IV fluids and nutrition	•Conservative approach. Use vasopressors preferentially rather than large volume (>30 mL/kg) IV fluid resuscitation; monitor renal functions. •Follow standard ICU protocols for nutritional support	

Supportive care	Actions	Explanatory notes
Nebulizer treatment	➢ Avoid nebulizers whenever possible to prevent aerosol spread ➢ Use MDIs for inhaled medications (including patients on MV) ➢ When required for some patients with asthma and COPD exacerbation, give nebulizers in an airborne infection isolation room	➢ If MDIs are not available, the patients may be able to use their own supply.

Pharmacotherapy	Actions
Implement ICU protocols for sedation, analgesia, neuromuscular blockade (if needed), stress ulcer prophylaxis, thromboembolism prophylaxis, glucose control	
Empiric antibiotics	For suspected bacterial co-infection **(elevated WBC, positive sputum culture, positive urinary antigen, atypical chest imaging),** administer empiric coverage for CAP or HAP
COVID-19-specific therapy	COVID-19 specific therapy, including ***dexamethasone, remdesivir, and interleukin-6 inhibitors*** should be considered. Therapies are evolving
Glucocorticoids for non-COVD-19 illnesses	•Give glucocorticoids for other indications (eg, asthma, COPD)

Adjustments to outpatient meds	Actions	Explanatory notes
Assess and seek expert consultation to manage comorbid conditions (asthma, COPD, sickle cell disease, immunocompromise, pregnancy)		
ICS	➢ For asthma, continue usual dose ➢ For COPD **without** asthmatic component or clear prior benefit, hold ICS ➢ For COPD **with** asthmatic component or clear prior benefit, continue ICS	
NSAIDs	•**Acetaminophen** is preferred antipyretic	•There are minimal data informing the risks of NSAIDs in the setting of COVID-19. Given the uncertainty, we use acetaminophen as the preferred antipyretic agent.
ACEi/ARBs	•Continue if there is no other reason for discontinuation (hypotension, acute kidney injury)	
Statins	•Patients taking a statin at baseline should continue	

Supportive care	Actions	Explanatory notes
O2 Res. support	➢ Goal SpO_2 88 to 96% ➢ May give NC up to 6 L/minute or NRB up to 10 L/minute ➢ Use of HFNC preferred over NIV. ✓ **1-use surgical mask over HFNC or NIV interfaces** **2-NIV may be preferred for indications with known benefit (eg, acute hypercapnia due to COPD exacerbation or ACHF)** **3-Reassess patients on HFNC and NIV every 1 to 2 hours, or sooner if SpO_2 <90 or clinical deterioration**	Some experts advocate placing a surgical mask on patients wearing low-flow oxygen devices, although the efficacy of this approach is unclear. It may be appropriate if the patient is not in an airborne isolation room or during transport.

Tracheal intubation and mechanical ventilation	Actions	Explanatory notes
Indications	➢ Rapid progression over hrs ➢ Persistent need for high flows/fraction of inspired O2 (eg, >60 L/minute) and FiO_2 >0.6 ➢ Evolving hypercapnia, increasing work of breathing, increasing TV, worsening mental status, increasing duration and depth of desaturations ➢ Hemodynamic instability or MOF	•Do **NOT** delay intubation until the patient has features of impending respiratory **arrest (RR>30/minutes, accessory muscle use, abdominal paradox) or is on maximum noninvasive supportive care** since this approach is potentially harmful to both the patient and healthcare workers

Tracheal intubation and MV	Actions	Explanatory notes
Rapid sequence intubation	➢ Performed by experienced intubator ➢ Avoid bag valve mask ventilation: If must perform, use in-line bacterial/viral filter; 2-person technique improves seal and reduces aerosolization.	
Ventilator settings	Provide low tidal volume ventilation: 1. AC with TV target 6 mL/kg IBW 2. PEEP/FiO_2: PEEP 10 to 15 cm H_2O to start 3. Titrate oxygen to target PaO_2 55 to 80/SpO_2 88 to 96 for most patients 4. Plateau pressure <30 cm H_2O	•ARDSNet provides a guide to PEEP and FiO_2 titration;.

Tracheal intubation and MV	Actions	Explanatory notes
Prone ventilation	➢ Suggest prone positioning should low TV ventilation fail (P/F ratio <150 mmHg × 12 hours, FiO_2 requirement ≥0.6, requirement for PEEP ≥5 cm H_2O) ➢ Advise daily prone position for 12 to 16 hours/day ➢ Need experienced staff; ensure that ETT and vascular access remain secured when turning	•Effects of prone ventilation typically seen over **4 to 8 hours**; improvements continue the longer it is used.

Tracheal intubation , MV	Actions	Explanatory notes
Additional rescue therapies	For patients who fail prone ventilation (P/F ratio <150 mmHg while prone), may consider the following interventions: ➢ **Recruitment maneuvers and high PEEP strategies** ➢ **Trial of inhaled pulmonary vasodilators such as NO/epoprostenol** ➢ **Neuromuscular blockade for patients with refractory hypoxemia (eg, P/F <100 mmHg) or ventilator dyssynchrony** ➢ **ECMO as a last resort; however, ECMO is not universally available**	➢ Pulmonary vasodilators should **not** be administered unless a specific protocol and staff experienced in their administration are in place. Inhaled vasodilators may increase aerosolization. ➢ Numerical improvement due to pulmonary vasodilators should not prevent prone positioning when otherwise indicated.

ARDS Mechanical Ventilation

NIH NHLBI ARDS Clinical Network
Mechanical Ventilation Protocol Summary

INCLUSION CRITERIA: Acute onset of

1. $PaO_2/FiO_2 \leq 300$ (corrected for altitude)
2. Bilateral (patchy, diffuse, or homogeneous) infiltrates consistent with pulmonary edema
3. No clinical evidence of left atrial hypertension

PART I: VENTILATOR SETUP AND ADJUSTMENT

1. Calculate predicted body weight (PBW)
   Males = 50 + 2.3 [height (inches) - 60]
   Females = 45.5 + 2.3 [height (inches) -60]
2. Select any ventilator mode
3. Set ventilator settings to achieve initial V_T = 8 ml/kg PBW
4. Reduce V_T by 1 ml/kg at intervals ≤ 2 hours until V_T = 6ml/kg PBW.
5. Set initial rate to approximate baseline minute ventilation (not > 35 bpm).
6. Adjust V_T and RR to achieve pH and plateau pressure goals below.

OXYGENATION GOAL: PaO_2 55-80 mmHg or SpO_2 88-95%

Use a minimum PEEP of 5 cm H_2O. Consider use of incremental FiO_2/PEEP combinations such as shown below (not required) to achieve goal.

Lower PEEP/higher FiO2

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 FiO2

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

PLATEAU PRESSURE GOAL: ≤ 30 cm H_2O

Check Pplat (0.5 second inspiratory pause), at least q 4h and after each change in PEEP or V_T.

If Pplat > 30 cm H_2O: decrease V_T by 1ml/kg steps (minimum = 4 ml/kg).

If Pplat < 25 cm H_2O and V_T< 6 ml/kg, increase V_T by 1 ml/kg until Pplat > 25 cm H_2O or V_T = 6 ml/kg.

If Pplat < 30 and breath stacking or dys-synchrony occurs: may increase V_T in 1ml/kg increments to 7 or 8 ml/kg if Pplat remains ≤ 30 cm H_2O.

ARDS Mechanical Ventilation

pH GOAL: 7.30-7.45

Acidosis Management: (pH < 7.30)

If pH 7.15-7.30: Increase RR until pH > 7.30 or $PaCO_2$ < 25 (Maximum set RR = 35).

If pH < 7.15: Increase RR to 35.

If pH remains < 7.15, V_T may be increased in 1 ml/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded).

May give $NaHCO_3$

Alkalosis Management: (pH > 7.45) Decrease vent rate if possible.

I: E RATIO GOAL: Recommend that duration of inspiration be ≤ duration of expiration.

PART II: WEANING

A. Conduct a SPONTANEOUS BREATHING TRIAL daily when:

1. $FiO_2 \leq 0.40$ and PEEP ≤ 8.
2. PEEP and FiO_2 ≤ values of previous day.
3. Patient has acceptable spontaneous breathing efforts. (May decrease vent rate by 50% for 5 minutes to detect effort.)
4. Systolic BP ≥ 90 mmHg without vasopressor support.
5. No neuromuscular blocking agents or blockade.

If all above criteria are met and subject has been in the study for at least 12 hours, initiate a trial of UP TO 120 minutes of spontaneous breathing with FiO2 ≤ 0.5 and PEEP ≤ 5:

1. Place on T-piece, trach collar, or CPAP ≤ 5 cm H_2O with PS ≤ 5
2. Assess for tolerance as below for up to two hours.
   a. $SpO_2 \geq 90$: and/or $PaO_2 \geq 60$ mmHg
   b. Spontaneous $V_T \geq 4$ ml/kg PBW
   c. RR ≤ 35/min
   d. pH ≥ 7.3
   e. No respiratory distress (distress= 2 or more)
      - HR > 120% of baseline
      - Marked accessory muscle use
      - Abdominal paradox
      - Diaphoresis
      - Marked dyspnea
3. If tolerated for at least 30 minutes, consider extubation.
4. If not tolerated resume pre-weaning settings.

Definition of UNASSISTED BREATHING

(Different from the spontaneous breathing criteria as PS is not allowed)

1. Extubated with face mask, nasal prong oxygen, or room air, OR
2. T-tube breathing, OR
3. Tracheostomy mask breathing, OR
4. CPAP less than or equal to 5 cm H_20 **without pressure support or IMV assistance.**

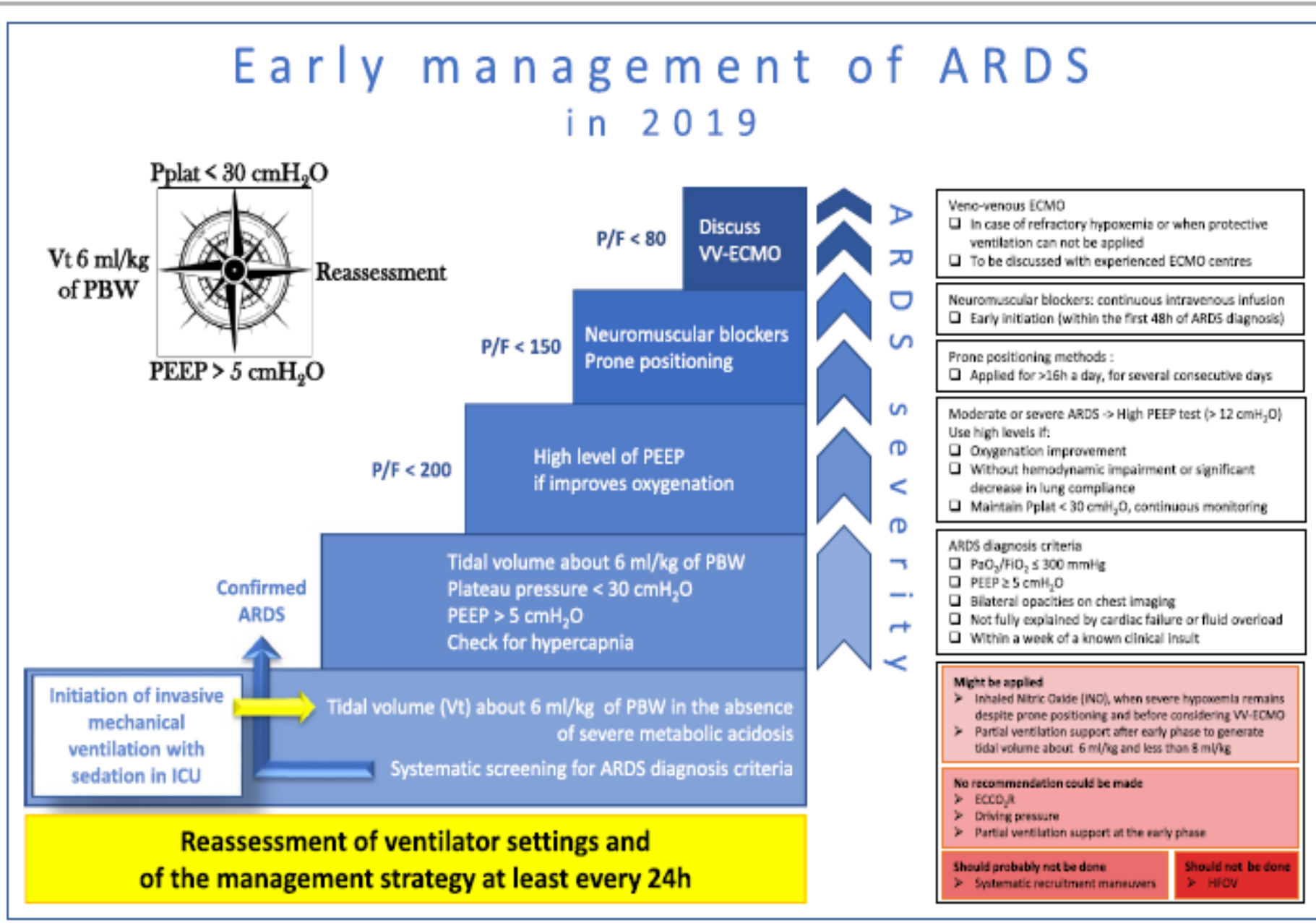
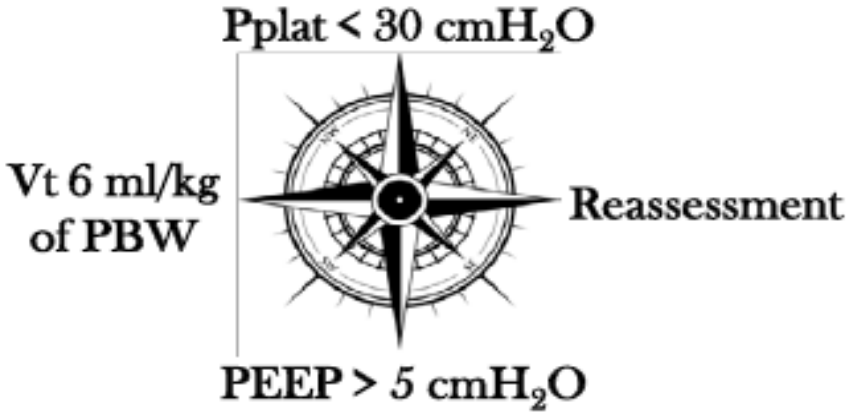


Fig. 1 Therapeutic algorithm regarding early ARDS management (EXPERT OPINION)



P/F < 80

Discuss VV-ECMO

P/F < 150

Neuromuscular blockers
Prone positioning

P/F < 200

High level of PEEP if improves oxygenation

Tidal volume about 6 ml/kg of PBW
Plateau pressure < 30 cmH_2O
PEEP > 5 cmH_2O
Check for hypercapnia

Confirmed ARDS

Initiation of invasive mechanical ventilation with sedation in ICU

Tidal volume (Vt) about 6 ml/kg of PBW in the absence of severe metabolic acidosis

Systematic screening for ARDS diagnosis criteria

ARDS severity

Reassessment of ventilator settings and of the management strategy at least every 24h

Sedation Management

The Society of Critical Care Medicine's (SCCM's) ICU Liberation Campaign promotes the ICU Liberation Bundle (A-F) to improve post-ICU patient outcomes.

The A-F Bundle includes the following elements:

A. **Assess, prevent, and manage pain**
B. **Both spontaneous awakening and breathing trials**
C. **Choice of analgesia and sedation**
D. **Delirium: assess, prevent, and manage**
E. **Early mobility and exercise**
F. **Family engagement and empowerment**

Post-Intensive Care Syndrome

1-prolonged delirium/encephalopathy use of mechanical ventilation; the use of restraints; the use of benzodiazepine, opioid, and vasopressor infusions; and the use of antipsychotics

Post-Intensive Care Syndrome

2- Neurological complications

- older age and underlying conditions, such as hypertension and diabetes mellitus
- Autopsy studies : both macrovascular and microvascular thrombosis, with evidence of hypoxic ischemia

Post-Intensive Care Syndrome

a spectrum of cognitive, psychiatric, and/or physical disability that affects survivors

1-profound muscle weakness (ICU-acquired weakness)

2- problems with thinking and judgment (cognitive dysfunction)

3-mental health problems, such as problems sleeping, post-traumatic stress disorder (PTSD), depression, and anxiety.

- ICU-acquired weakness affects 33% of all patients who receive mechanical ventilation, 50% of patients with sepsis, and ≤50% of patients who remain in the ICU for ≥1 week.
- Cognitive dysfunction affects 30% to 80% of patients discharged from the ICU.
- About 50% of ICU survivors do not return to work within 1 yr

Post-Intensive Care Syndrome

minimize the risk of PICS through

1-medication management (using the A-F Bundle)

2-physical rehabilitation

3-follow-up clinics

4-family support

5-improved education about the syndrome.

Mechanical Ventilation in COVID-19 Patients: Insights into the Role of Age and Frailty from a Multicentre Observational Study

Fiona Ecarnot[1*], Paola Rebora[2], Emanuele Focà[3], Alberto Zucchelli[4], Giuseppe Citerio[5,6], Maria Grazia Valsecchi[2], Alessandra Marengoni[7,#], Giuseppe Bellelli[5,8,#], for the FRACoViD Team

[1]EA3920, University of Franche-Comté and Department of Cardiology, University Hospital Besançon, Besançon, France. [2]Bicocca Center of Bioinformatics, Biostatistics and Bioimaging, School of Medicine and Surgery, University of Milano-Bicocca, Monza, Italy. [3]Department of Clinical and Experimental Sciences, University of Brescia, and Division of Infectious and Tropical Diseases, Spedali Civili Hospital, Brescia, Italy. [4]Department of Information Engineering, University of Brescia, Brescia, Italy. [5]School of Medicine and Surgery, University of Milano – Bicocca, Italy. [6]Neuro Intensive Care, San Gerardo hospital, ASST-Monza, Monza Italy.[7]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy. [8]Acute Geriatric Unit, San Gerardo hospital, Monza, Italy.

[Received January 5, 2022; Revised January 25, 2022; Accepted January 27, 2022]

- *Frailty Index (FI) = (number of health deficits present) ÷ (number of health deficits measured)*
- For example, a person with 20 of 40 deficits collected has an FI score of 20/40 = 0.5; whilst for someone with 10 deficits, the FI score is 10/40 = 0.25.

Week grip strength	Cut off points for grip strength of the dominant hand is as following, =17 kg for BMI =23 =17.3 kg for BMI 23 < BMI 26 =18 kg for BMI 26 < BMI 29 =21 kg for BMI >29
Slow gait speed	The subject could use a walking aid, but not the aid of another person. Walking 4m (speed) in: =0.65 m/s for height =159cm =0.76 m/s for height >159 cm
Low physical activity level	Global Physical Activity Questionnaire (GPAQ) according to WHO (2012) recommendation was used to determine the physical activity level.
Self-reported exhaustion	Indicative positive response of any one out of three questions. a. Felt unusually tired in the previous month? (low energy level <3 {on of scale of 0–10}) b. Felt unusually weak in the previous month? c. Had an unusually low energy level? (For b. and c., most or all the time {where, rarely [<1day], some or little of the time [1–2 days], most of the time [3–4 days] and all the time})
Low weight	BMI <18.5 kg/m², which is the lowest category WHO BMI classification.

List of 40 Variables included in the frailty index	Cut Point
Help Bathing	Yes = 1, No = 0
Help Dressing	Yes = 1, No = 0
Help getting in/out of Chair	Yes = 1, No = 0
Help Walking around house	Yes = 1, No = 0
Help Eating	Yes = 1, No = 0
Help Grooming	Yes = 1, No = 0
Help Using Toilet	Yes = 1, No = 0
Help up/down Stairs	Yes = 1, No = 0
Help lifting 10 lbs	Yes = 1, No = 0
Help Shopping	Yes = 1, No = 0
Help with Housework	Yes = 1, No = 0
Help with meal Preparations	Yes = 1, No = 0
Help taking Medication	Yes = 1, No = 0
Help with Finances	Yes = 1, No = 0
Lost more than 10 lbs in last year	Yes = 1, No = 0
Self Rating of Health	Poor = 1, Fair = 0.75, Good = 0.5, V. Good = 0.25, Excellent = 0
How Health has changed in last year	Worse = 1, Better/Same = 0
Stayed in Bed at least half the day due to health (in last month)	Yes = 1, No = 0
Cut down on Usual Activity (in last month)	Yes = 1, No = 0
Walk outside	<3 days = 1, ≤ 3 days = 0
Feel Everything is an Effort	Most of time = 1, Some time = 0.5, Rarely = 0
Feel Depressed	Most of time = 1, Some time = 0.5, Rarely = 0
Feel Happy	Most of time = 0, Some time = 0.5, Rarely = 1
Feel Lonely	Most of time = 1, Some time = 0.5, Rarely = 0
Have Trouble getting going	Most of time = 1, Some time = 0.5, Rarely = 0
High blood pressure	Yes = 1, Suspect = 0.5, No = 0
Heart attack	Yes = 1, Suspect = 0.5, No = 0
CHF	Yes = 1, Suspect = 0.5, No = 0
Stroke	Yes = 1, Suspect = 0.5, No = 0
Cancer	Yes = 1, Suspect = 0.5, No = 0
Diabetes	Yes = 1, Suspect = 0.5, No = 0
Arthritis	Yes = 1, Suspect = 0.5, No = 0
Chronic Lung Disease	Yes = 1, Suspect = 0.5, No = 0
MMSE	<10 = 1, 11–17 = 0.75, 18–20 = 0.5, 20–24 = 0.25, >24 = 0
Peak Flow	See Table 2
Shoulder Strength	See Table 2
BMI	See Table 2
Grip Strength	See Table 2
Usual Pace	See Table 2
Rapid Pace	See Table 2

1. **score 0 to 0.12** represents patients without frailty
2. **>0.12 to 0.24** represents patients with mild frailty
3. **>0.24 to 0.36** represents patients with moderate frailty
4. **>0.36** represents patients with severe frailty

QJM: An International Journal of Medicine, 2021, 182–189

doi: 10.1093/qjmed/hcab029
Advance Access Publication Date: 12 February 2021
Original paper

ORIGINAL PAPER

Should COVID-19 patients >75 years be Ventilated? An Outcome Study

H. Raheja [1], N. Chukwuka [2], C. Agarwal [1], D. Sharma [2], A. Munoz-Martinez [2], J. Fogel [3], M. Khalid [1], A. T. Hashmi [1], S. Ehrlich [2], M. A. Waheed [2], S. Siddiqui [1], B. A. de Brito Gomes [2], A. Aslam [2], C. J. Merino Gualan [4], I. Aftab [2], A. Tiwari [2], S. Singh [2], K. Pouching [2], N. Somal [2], J. Shani [1] and G. Rojas-Marte [1,5]

Results: A total of 355 patients aged ≥75 years hospitalized with COVID-19 between 19 March and 25 April 2020 were included.Mean age was 84.3 years. One-third of the patients developed critical disease. Mean length of stay was 7.10 days. Vasopressors were required in 27%, with the highest frequency in the critical disease group (74.1%). Overall mortality was 57.2%, with a significant difference between severity groups (mild/moderate disease: 17.4%, severe/very severe disease: 71.3%, critical disease: 94.9%, $P < 0.001$).Increased age, dementia, and severe/very severe and critical disease groups were independently associated with increased odds for mortality while diarrhea was associated with decreased odds for mortality (OR: 0.12, 95% CI: 0.02–0.60, $P < 0.05$). None of the cardiovascular comorbidities were significantly associated with mortality.
Conclusion: Age and dementia are associated with increased odds for mortality in patients ≥75 years of age hospitalized with COVID-19. Those who require intubation have the greatest odds for mortality. Diarrhea as a presenting symptom was associated with lower odds for mortality.

Received: 12 October 2021 | Revised: 20 January 2022 | Accepted: 6 February 2022
DOI: 10.1111/jgs.17718

CLINICAL INVESTIGATION

Journal of the
American Geriatrics Society

Factors associated with hospital admission and severe outcomes for older patients with COVID-19

- For patients aged 85+:

the five risk factors with the highest attributable fractions of COVID-19 severe outcomes:

1-frailty

2- chronic kidney disease

3-male sex

4-heart failure

5-dementia.

- Only **dementia** increased in importance for COVID-19 outcomes with increasing age, while most comorbidities and biomarkers showed decreased effect with age.
- Patients of COVID-19, especially older patients, without ambulatory care histories had significantly higher rates of hospitalization and severe outcomes.

Received: 12 October 2021 | Revised: 20 January 2022 | Accepted: 6 February 2022
DOI: 10.1111/jgs.17718

CLINICAL INVESTIGATION

Journal of the
American Geriatrics Society

Factors associated with hospital admission and severe outcomes for older patients with COVID-19

With increasing age, the attributable risk fractions decreased for sex, race–ethnicity, and most comorbidities,

while increased for

dementia

heart failure

frailty

Important post-acute clinical events occur among nursing home residents who have survived COVID-19, including:

geriatric syndromes such as

Falls

Delirium

progression of frailty

all of which affect quality of life and are important

Wei et al. BMC Geriatrics (2020) 20:395
https://doi.org/10.1186/s12877-020-01811-5

BMC Geriatrics

RESEARCH ARTICLE Open Access

Clinical characteristics and manifestations in older patients with COVID-19

Chenchen Wei[1], Ya Liu[2], Yapeng Liu[1], Kai Zhang[1,3], Dezhen Su[3], Ming Zhong[1] and Xiao Meng[1,3*]

older patients had

1-more underlying comorbidities and laboratory abnormalities

2- A higher rate of :
- **ARDS**
- **acute cardiac injury**
- **heart failure was observed**

particularly those oldest-old patients had more MOF

Multivariable analysis showed:

age, lymphopenia, ARDS, acute cardiac injury, heart failure and skeletal muscle injury were

associated with death in older patients

while glucocorticoids might be harmful

Singhal et al. BMC Geriatrics (2021) 21:321
https://doi.org/10.1186/s12877-021-02261-3

BMC Geriatrics

RESEARCH ARTICLE Open Access

Clinical features and outcomes of COVID-19 in older adults: a systematic review and meta-analysis

Sunny Singhal[1], Pramod Kumar[1], Sumitabh Singh[2], Srishti Saha[3] and Aparajit Ballav Dey[1]*

Forty-six studies with 13,624 older patients

- **Severe infection :51%**
- **critically ill: 22%**
- **died :11%**

- The common comorbidities:
  - hypertension
  - diabetes mellitus
  - cardiovascular disease
- **Common symptoms were fever ,cough ,dyspnoea**
- **84% required oxygen support**
  21% required mechanical ventilation
- **half:severe infection**
  one in five:critically ill
  one in ten: die

WJCCM World Journal of Critical Care Medicine

Submit a Manuscript: https://www.f6publishing.com

World J Crit Care Med 2021 September 9; 10(5): 278-289

DOI: 10.5492/wjccm.v10.i5.278

ISSN 2220-3141 (online)

SYSTEMATIC REVIEWS

Elderly adults with COVID-19 admitted to intensive care unit: A narrative review

- studies involving 17011 ICU patients
- Among the whole patient population, included in these studies, 8310 patients were older than 65 years of age and 2630 patients were older than 70 years.
- They suffered from **more comorbidities** and showed a varied, albeit **high mortality**.
- The evidence so far suggests that **advanced age** and **comorbidities** are associated with worse clinical outcome.

Clinical presentation of COVID-19 cases due to Delta and Omicron variant (April 2022)

Symptoms of upper respiratory tract infection (URI) are **the most common manifestations of non severe COVID-19**

- In an observational study evaluating the reported clinical symptoms of over 63,000 confirmed COVID-19 cases between two time periods (during Delta variant predominance and Omicron variant predominance), **nasal congestion, headache, sneezing, and sore throat**

the most common presenting symptoms

Sore throat was more common and **alteration or loss of smell was less common** during the time period of Omicron predominance

As new variants emerge, the predominant URI symptoms of COVID-19 may continue to change.