

A Neurosurgeon's Guide to Cardiovascular and Renal Critical Care for COVID-19

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Introduction

As the number of people infected with the novel **coronavirus** rapidly increases, some neurosurgeons are being asked to participate in the **care of critically ill patients**, even those without neurological involvement. This presentation is meant to be a basic guide to help neurosurgeons achieve this mission.

Disclaimer

- The protocols discussed in this presentation are from the **Mission: Possible** program at **University Hospitals of Cleveland**, based on guidelines and recommendations from several medical societies and the Centers for Disease Control (CDC).
- Please check with your own hospital or institution to see if there is any variation from these protocols before implementing them in your own practice.

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COVID-19

- Coronavirus disease 2019 (COVID-19) is a respiratory tract infection caused by a newly emergent coronavirus, SARS-CoV-2, that was first recognized in Wuhan, China, in December 2019.
- Genetic sequencing of the virus suggests that SARS-CoV-2 is a betacoronavirus closely linked to the SARS.

Personal Protective Equipment

When taking care of COVID-19 patients, please adhere to all of your institution's policies regarding personal protective equipment (PPE)

To help others, you must **stay healthy** yourself!

Aerosol Generating Procedures in ICU

PPE = Fit tested respirator N95 or PAPR + Eye Protection with face shield or Goggles + Gown + Gloves		
Intubation	Extubation	Airway surgeries – ENT, Thoracic Transsphenoidal
Open Suctioning	Nebulizer therapy	Procedures in agitated patients
Sputum induction	Manual Bag-mask ventilation	Chest physical therapy
CPR	Bronchoscopy	Mechanical In-Exsufflator [Cough Assist Device]
NIV	Tracheostomy	Upper and Lower Endoscopy
Hi Flow O2	Tracheostomy change	Ventilator circuit manipulation

Organ System Interactions

While this guide focuses on organ pathophysiology and treatment, it should be remembered that each organ system interacts with the others. Sometimes the best treatment of one organ is detrimental to another. It is always important to do what is **best for the whole organism**, not just one organ.

Organ System Interactions

For example, consider a patient with systolic heart failure with pulmonary edema and hypoxic respiratory failure who also has an acute kidney injury with oliguria. While the best treatment for the hypoxia might be diuresis to reduce the pulmonary edema, this could worsen the kidney injury and push this patient into renal failure with the need for dialysis. This would decrease the chances of recovery. A better strategy might be to increase PEEP to improve oxygenation while the kidney injury resolves.

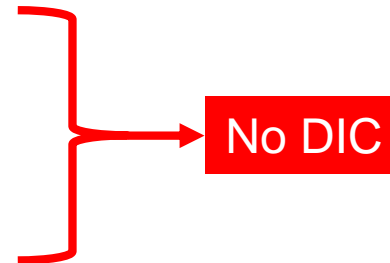
COVID-19 Infection in ICU

In addition to the hypoxic respiratory failure, several organ and physiologic derangements are observed.

- Marked increase in acute phase reactants
- Venous thromboembolic disease
- Hemodynamic instability
- Cardiac Dysfunction
- Acute Kidney Injury

COVID-19 - Hematologic Profile

- Several pro-coagulant factors are increased
 - Factor VIII
 - VWF
 - Fibrinogen known to be associated with an increased risk of thrombosis
- Increased D-Dimer suggestive of local on going fibrinolysis
- Normal platelet counts
- Normal PT and PTT



Venous Thromboembolic Disease

Common in the ICU population

- Immobility
- Prothrombotic conditions
 - Reports of higher rates of thrombosis with COVID-19

Conditions

- Deep vein thrombosis (DVT)
- Pulmonary embolism (PE)
- Sagittal sinus thrombosis

DVT Risk Assessment

VENOUS THROMBOEMBOLISM RISK ASSESSMENT AND PROPHYLAXIS GUIDELINE FOR ADULT PATIENTS²⁵⁻²⁷

Risk assessment methods	<ul style="list-style-type: none"> • Each factor listed with a point score • Add points based on factor(s) to determine risk factor score • Choose recommended prophylaxis based on total score in conjunction with clinical judgment 		
Factors	<p>PATIENT FACTORS (points value)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Age over 75 years (3) <input type="checkbox"/> Age 60-74 years (2) <input type="checkbox"/> Age 41-60 years (1) <input type="checkbox"/> BMI 26-34.9 (1) <input type="checkbox"/> BMI 35-39.9 (3) <input type="checkbox"/> BMI 40-49.9 (3) <input type="checkbox"/> BMI 50 or > (3) <input type="checkbox"/> Central Venous Access (2) <input type="checkbox"/> Patient Confined to Bed > 72 hrs (2) <input type="checkbox"/> Bed rest (1) <input type="checkbox"/> Swollen legs, current (1) <input type="checkbox"/> Varicose veins (1) <p>TOTAL POINTS: <input type="checkbox"/></p>	<p>MEDICAL FACTORS (points value)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Malignancy, present or previous (2) <input type="checkbox"/> Acute myocardial infarction (1) <input type="checkbox"/> CHF, <1 month (1) <input type="checkbox"/> Inflammatory Bowel Disease (1) <input type="checkbox"/> COPD (1) <input type="checkbox"/> Serious lung disease incl. pneumonia, < 1 month (1) <input type="checkbox"/> Sepsis, < 1 month (1) <p>TOTAL POINTS: <input type="checkbox"/></p>	<p>SURGICAL FACTORS (points value)</p> <ul style="list-style-type: none"> <input type="checkbox"/> New TRAUMA admission (5) <input type="checkbox"/> Multiple Trauma, < 1 month (5) <input type="checkbox"/> Elective Major Lower Extremity Arthroplasty (5) <input type="checkbox"/> Hip, Pelvis, or Leg Fracture, < 1 month (5) <input type="checkbox"/> Immobilizing Plaster Cast (2) <input type="checkbox"/> Current Major Surgery, >45 min (2) <input type="checkbox"/> Current Minor Surgery, <45 min/History of Prior Major Surgery < 1 month (1) <p>TOTAL POINTS: <input type="checkbox"/></p>
	<p>OB/GYN FACTORS (points value)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Pregnancy intrapartum (2) <input type="checkbox"/> Pregnancy antepartum or postpartum (2) <input type="checkbox"/> Oral Contraceptives or Hormone Replacement Therapy (1) <p>TOTAL POINTS: <input type="checkbox"/></p>	<p>NEUROLOGIC FACTORS (points value)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Acute Spinal Cord Injury, Paralysis, < 1 month (5) <input type="checkbox"/> Stroke, < 1 month (5) <p>TOTAL POINTS: <input type="checkbox"/></p>	<p>COAGULATION FACTORS</p> <ul style="list-style-type: none"> <input type="checkbox"/> History of DVT/PE (3) <input type="checkbox"/> Family history of thrombosis (3) <input type="checkbox"/> HIT Heparin –induced thrombocytopenia (3) <input type="checkbox"/> Other congenital or acquired thrombophilia - positive Factor V Leiden, positive Prothrombin 20210A, elevated serum homocysteine, positive lupus anticoagulant, elevated anticardiolipin antibodies (3) <p>TOTAL POINTS: <input type="checkbox"/></p>
Total risk factor score	<p style="text-align: right;">_____ POINTS</p>		

Usual VTE Prophylaxis

■ Most ICU patients will be high risk

- **HIGHEST RISK (≥ 5 or more points)**
 - One pharmacologic option **AND** intermittent pneumatic compression
 - Use nonpharmacologic options as sole prophylaxis for patients not candidates for anticoagulant therapy
 - Enoxaparin 40 mg SC daily
 - Enoxaparin 30 mg SC daily if CrCL < 30 mL/min AND not on dialysis
 - Unfractionated heparin 5,000 units SC Q8H
 - Fondaparinux 2.5 mg SC daily
 - Intermittent pneumatic compression
- **BMI ≥ 40 kg/m²**
 - One pharmacologic option **AND** intermittent pneumatic compression
 - Use nonpharmacologic options as sole prophylaxis for patients not candidates for anticoagulant therapy
 - Enoxaparin 40 mg SC Q12H (if BMI $\geq 40 - 49.9$ kg/m²)
 - Enoxaparin 60 mg SC Q12H (if BMI ≥ 50 kg/m²)
 - Unfractionated heparin 7,500 units SC Q8H
 - Fondaparinux 2.5 mg SC daily
 - Intermittent pneumatic compression

VTE Prophylaxis

Prophylaxis may be held for high risk of bleeding

- Ongoing or recent severe hemorrhage
- Thrombocytopenia (platelets <100,000)
- Renal failure, end stage liver disease
- Coagulopathy
- Currently on anticoagulation therapy

COVID-19 Venous Thromboembolic Disease

- Standard prophylaxis is not adequately preventing thromboembolic events
- Several reports
 - Pulmonary embolism
 - Arterial thrombosis
 - Strokes
 - Thrombosis in unusual areas
 - Microthrombi in lungs on autopsy series

J Thromb Haemost. April 2020

VTE Prophylaxis in COVID-19 Patients

STEP I – Calculate DIC Score

ISTH Criteria for DIC - 5 points are needed for DIC Diagnosis

Platelets	50-100 K	1 point	If score is ≥ 5 – DIC is diagnosed – hematology consult	
	< 50 K	2 points		
D-Dimer	1000-3000 ng/ml	1 point		
	> 3000 ng/ml	3 points		
Fibrinogen	< 100 mg/dl	1 point		If score is < 5 – there is no DIC – proceed to STEP II
Prolonged PT	3-6 seconds	1 point		
	> 6 seconds	2 points		

- STEP II – POC ultrasound of lower extremities
 - DVT present – full anticoagulation
 - NO DVT – proceed to STEP III

University Hospitals COVID-19 DVT prophylaxis protocol

STEP III - VTE prophylaxis

D- Dimer ng/ml	Weight (kg)	Drug <u>target Heparin Assay, Lovenox is 0.2 – 0.4 IU/mL</u>
< 1000	< 100	Enoxaparin 40 mg qd
	100-150	Enoxaparin 40 mg bid
	> 150	Enoxaparin 60 mg bid
	<ul style="list-style-type: none"> ▪ Enoxparin should be timed for 0900 (and 2100 if BID) ▪ Heparin Assay, Lovenox should be drawn 4 hours after the second dose, then as needed based on level and renal function <ul style="list-style-type: none"> ○ Adjust doses in increments of 10 – 20 mg depending on level and renal function ▪ If on CRRT or HD, <ul style="list-style-type: none"> ○ use heparin 5,000 Units Q8H when weight < 150 Kg ○ use heparin 7,500 Units Q8H when weight > 150 Kg 	

D- Dimer ng/ml	Weight (kg)	Drug <u>target Heparin Assay, Lovenox is 0.2 – 0.4 IU/mL</u>
1000 - 3000	< 100	Enoxaparin 40 mg bid
	100-150	Enoxaparin 80 mg bid
	> 150	Enoxaparin 120 mg bid
	<ul style="list-style-type: none"> ▪ For doses ≥ 80 mg, may need to use the “<i>Enoxaparin Therapeutic Anticoagulation</i>” UHCare orderset for ease of ordering higher doses ▪ Enoxparin should be timed for 0900 and 2100 ▪ Heparin Assay, Lovenox should be drawn 4 hours after the second dose, then as needed based on level and renal function <ul style="list-style-type: none"> ○ Adjust doses in increments of 10 – 20 mg depending on level and renal function ▪ If on CRRT or HD, use low intensity unfractionated Heparin drip 	

University Hospitals COVID-19
DVT prophylaxis protocol

D- Dimer ng/ml	Weight (kg)	Drug <u>target Heparin Assay, 0.4 -0.7 IU/ml</u>
> 3000	<ul style="list-style-type: none"> ▪ In absence or renal failure and morbid Obesity use Enoxaparin 1 mg/Kg every 12 hr ▪ OR ▪ Start with Hi intensity unfractionated Heparin drip – as per EMR ▪ If no improvement in D-Dimer in 24-48 consult hematology and/or vascular medicine 	

Pulmonary Embolism (PE): Definitions

Massive PE	Submassive PE	Minor/Nonmassive PE
High risk	Moderate/intermediate risk	Low risk
<ul style="list-style-type: none"> • Sustained hypotension (systolic BP <90 mmHg for ≥ 15 min) • Inotropic support • Pulseless • Persistent profound bradycardia (HR <40 bpm with signs or symptoms of shock) 	<ul style="list-style-type: none"> • Systemically normotensive (systolic BP ≥ 90 mmHg) • RV dysfunction • Myocardial necrosis 	<ul style="list-style-type: none"> • Systemically normotensive (systolic BP ≥ 90 mmHg) • No RV dysfunction • No myocardial necrosis



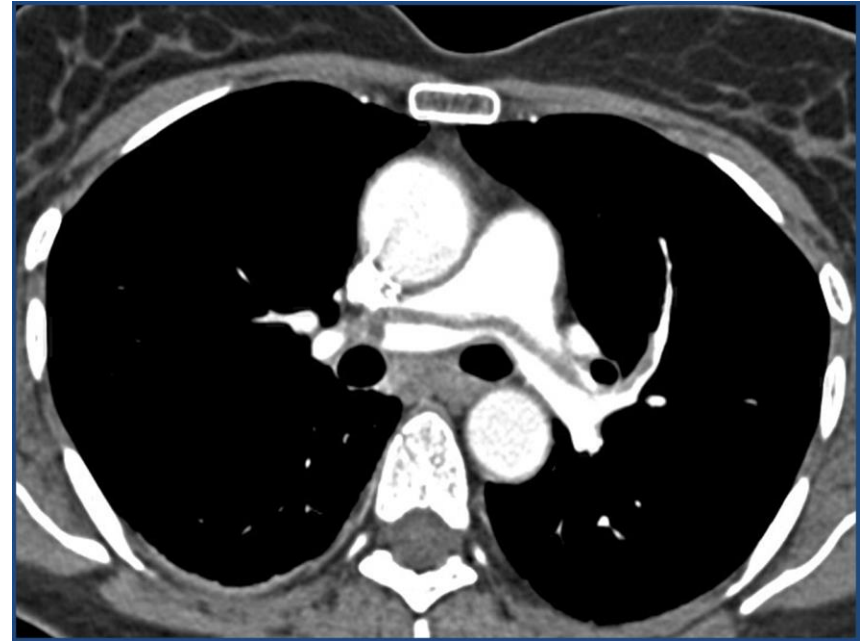
RV dysfunction suspected

- RV/LV ratio > 0.9 or RV systolic dysfunction on echo
- RV/LV ratio > 0.9 on CT
- Elevation of BNP (>90 pg/mL)
- Elevation of NTpro-BNP (>500 pg/mL)
- ECG changes:
 - new complete or incomplete RBBB
 - anteroseptal ST elevation or depression
 - anteroseptal T-wave inversion



Physiologic Effects of PE

- Impaired gas exchange in all types
 - V/Q mismatch, elevated A-a gradient
 - hypercapnia usually not present
 - functional shunting
- Hypotension in massive or submassive PE
 - decreased pre-load, if RV can't manage
 - increased pulmonary vascular resistance
 - RV strain (seen on EKG or echo)
 - Rise in troponin and BNP reflect the degree of RV injury. Lactic acidosis reflect severity of shock



Diagnosis of Pulmonary Embolism

- Evaluate hypoxia
 - Chest x-ray to look for parenchymal disease that may explain hypoxemia
 - Arterial blood gas to evaluate A-a gradient
- Spiral contrasted chest CT
- **Cannot perform V/Q scan** because of risk of viral spread from inhaled tracer

Treatment of PE

- ABC's always
- Fluids, pressors, ventilator management
 - hydration sparingly, can worsen right heart strain
 - avoid tachycardia, can worsen hypotension
 - further decrease in pre-load
 - be careful with plateau pressures
- PE Response Team (PERT) if available at your institution to navigate for the optimal therapeutic intervention

Pulmonary Embolism Treatment

- Anticoagulation
 - Goal PTT 50-70
 - Goal Factor Xa 0.3-0.8
 - Goal INR 2-3
- IVC filter to prevent subsequent PE if anticoagulation is not an option
- For massive PE or if anticoagulation is contraindicated
 - Thrombectomy – by cardiac catheterization or surgical
 - Systemic Thrombolysis: for life-threatening PE
 - 50 mg i.v., may repeat x1
 - Catheter directed thrombolysis

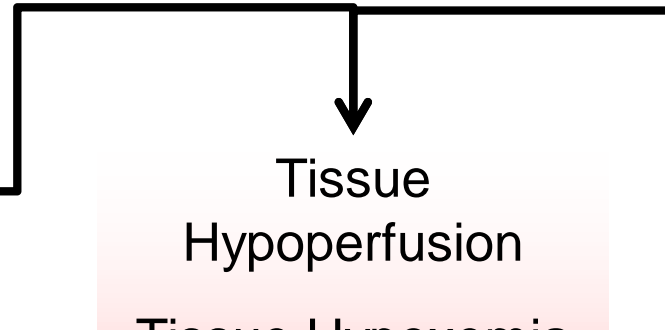
Hemodynamic Instability

Distributive

Sepsis
Anaphylaxis
Spinal

Cardiogenic

Myocardial Infarct
Heart Failure
Valve D/O



Hypovolemic

Hemorrhage
Trauma
Dehydration

Tissue Hypoxemia
Anaerobic Metabolism
Lactic Production
End-Organ Injury

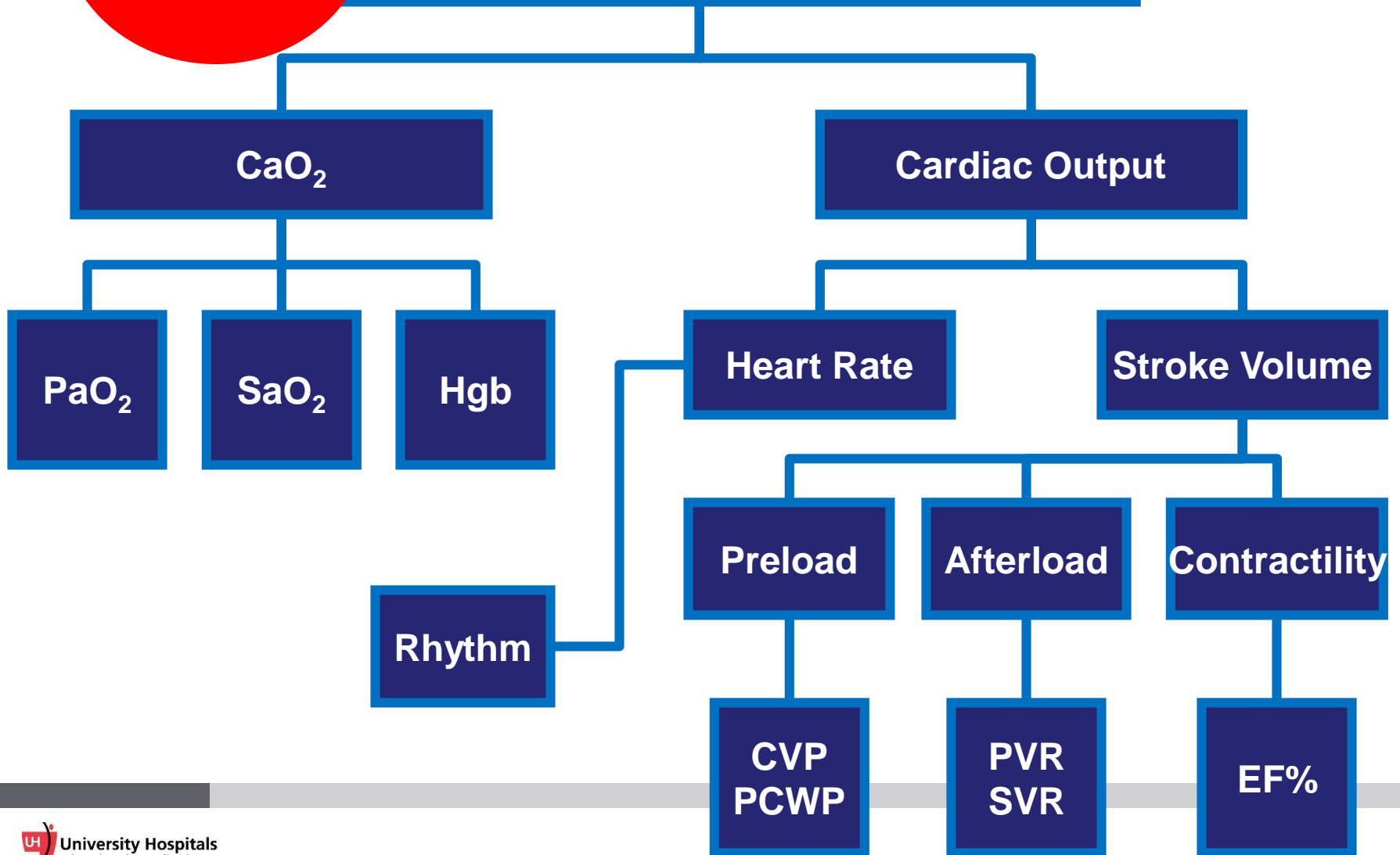
Obstructive

Pulmonary Embolism
Cardiac Tamponade

Multi-System
Organ Dysfunction

In Shock
Optimize
DO₂

Oxygen Delivery

$$DO_2 = CaO_2 \times CO$$


Stepwise Approach to Evaluate Shock

- Step 1: Clinical assessment
- Step 2: Volume status
- Step 3: Preload and fluid responsiveness
- Step 4: Cardiac output
- Step 5: Cardiac contractility
- Step 6: Differentiate shock state

Hemodynamic Goals in COVID-19

- Goal is **euvolemia** – WHO and ARDSnet recommended FACTT Algorithm
- Attempt de-resuscitation within 24-48 hours of achieving stability
- Point of care ultrasound of IVC and cardiac output maybe utilized in selected patients
- Pharmacy to concentrate all i.v. medications
- Enteral fluids to be determined on case by case basis by intensivist

Normal Cardiac Parameters

- Cardiac Output ($CO = HR \times \text{stroke volume}$)
Normal 4-8 L/min
- Cardiac Index ($CI = CO/\text{body surface area}$)
Normal 3-5 L/min/m²
- CVP
Normal 1-6 mm Hg
- Pulmonary artery pressure
Normal 16-24/5-12 mmHg

Hemodynamic Monitoring

■ Echocardiogram

- Heart chamber morphology and contractility (ejection fraction)
- Cardiac valve function
- Vena cava collapse (sign of hypovolemia)
- Estimates pulmonary artery pressure (may relate left ventricular filling and subsequently cardiac output)

■ Central venous catheter

- Central venous pressure

■ Pulmonary artery catheter (Swan-Ganz)

- **Not for routine use.** Reserve for patients with Pulmonary HTN and advanced heart failure
- Measures right ventricular pressures
- Measures PA wedge pressure
- Estimates cardiac output

Shock

	Intravascular Volume Status	Cardiac Output	Systemic Vascular Resistance
Distributive	↓	↑	↓
Hypovolemic	↓	↑	↑
Cardiogenic		↓	↑
Neurogenic		↓	↓

Adrenergic Receptors

- α_1 Smooth muscle contraction
- α_2 CNS inhibition
- β_1 Cardiac inotropy and chronotropy
- β_2 Smooth muscle relaxation

Medication	Usual Infusion Dose	Receptor Binding				Hemodynamic Effects
		α_1	β_1	β_2	Dopamine	
Vasopressor/inotropes						
Dopamine	0.5–2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	–	+	–	+++	$\uparrow\text{CO}$
	5–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+	+++	+	++	$\uparrow\uparrow\text{CO}$, $\uparrow\text{SVR}$
	10–20 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+++	++	–	++	$\uparrow\uparrow\text{SVR}$, $\uparrow\text{CO}$
Norepinephrine	0.05–0.4 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	++++	++	+	–	$\uparrow\uparrow\text{SVR}$, $\uparrow\text{CO}$
Epinephrine	0.01–0.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	++++	++++	+++	–	$\uparrow\uparrow\text{CO}$, $\uparrow\uparrow\text{SVR}$
Phenylephrine	0.1–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+++	–	–	–	$\uparrow\uparrow\text{SVR}$
Vasopressin	0.02–0.04 U/min	Stimulates V_1 receptors in vascular smooth muscle				$\uparrow\uparrow\text{SVR}$, $\leftrightarrow\text{PVR}$
Inodilators						
Dobutamine	2.5–20 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	+	++++	++	–	$\uparrow\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Isoproterenol	2.0–20 $\mu\text{g}/\text{min}$	–	++++	+++	–	$\uparrow\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Milrinone	0.125–0.75 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Enoximone	2–10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$
Levosimendan	0.05–0.2 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Myofilament Ca^{2+} sensitizer, PD-3 inhibitor				$\uparrow\text{CO}$, $\downarrow\text{SVR}$, $\downarrow\text{PVR}$

CO indicates cardiac output; CS, cardiogenic shock; PD-3, phosphodiesterase-3; PVR, pulmonary vascular resistance; and SVR, systemic vascular resistance.

Circulation 2017;136:e232-e268

Sepsis – 3 Clinical Identification

- Outside ICU - Known or presumed active infection who are likely to have poor outcomes can be identified by Sequential Organ Failure Assessment (SOFA)
 - SBP <100 mmHg
 - RR > 22
 - Altered mental status (encephalopathy)
- ICU patients with suspected or presumed infection who are likely to have poor outcomes can be identified by 2 or more SOFA points
- Septic shock
 - Despite adequate fluid resuscitation pressors are needed to maintain MAP > 65 **AND**
 - Serum Lactate > 2 mmol/L

SOFA Score

	Score				
System	1	2	3	4	5
<u>Respiration</u> PaO ₂ /FiO ₂ mmHg	<400	<400	<300	<200 with respiratory support	<100 with respiratory support
<u>Coagulation</u> Platelets, x10 ³ /μl	≥150	<150	<100	<50	<20
<u>Liver</u> Bilirubin mg/dL	<1.2	1.2-1.9	2-5.9	6-11.9	>12
<u>Cardiovascular</u>	MAP≥70 mmHg	MAP<70 mmHg	Dopamine<5 or dobutamine (any dose)	Dopamine 5.1-15 or epinephrine≤0.1 or norepinephrine≤0.1	Dopamine >15 Or epinephrine>0.1 or norepinephrine>0.1
<u>CNS</u> GCS	15	13-14	10-12	6-9	<6
<u>Renal</u> Creatinine mg/dL Urine Output mL/day	<1.2	1.2-1.9	2-3.4	3.5-4.9 <500	>5 <200

Sepsis Management Outline

Initial resuscitation	Fluid therapy	
Infection issues	Diagnoses Infection prevention	Antimicrobial therapy Source control
Hemodynamic support	Fluid therapy Vasopressors	Inotropic support Blood products
Adjunctive therapy	Corticosteroids	
Supportive measures	Mechanical ventilation Sedation, analgesia and neuromuscular blockade	Glucose control RRT Nutrition and prophylaxis



Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes^{1*}, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵, Ricard Ferrer⁶, Anand Kumar⁷, Jonathan E. Sevransky⁸, Charles L. Sprung⁹, Mark E. Nunnally², Bram Rochwerg³, Gordon D. Rubinfeld¹⁰, Derek C. Angus¹¹, Djillali Annane¹², Richard J. Beale¹³, Geoffrey J. Bellinghan¹⁴, Gordon R. Bernard¹⁵, Jean-Daniel Chiche¹⁶, Craig Coopersmith⁸, Daniel P. De Backer¹⁷, Craig J. French¹⁸, Seitaro Fujishima¹⁹, Herwig Gerlach²⁰, Jorge Luis Hidalgo²¹, Steven M. Hollenberg²², Alan E. Jones²³, Dilip R. Karnad²⁴, Ruth M. Kleinpell²⁵, Younsuk Koh²⁶, Thiago Costa Lisboa²⁷, Flavia R. Machado²⁸, John J. Marini²⁹, John C. Marshall³⁰, John E. Mazuski³¹, Lauralyn A. McIntyre³², Anthony S. McLean³³, Sangeeta Mehta³⁴, Rui P. Moreno³⁵, John Myburgh³⁶, Paolo Navalesi³⁷, Osamu Nishida³⁸, Tiffany M. Osborn³¹, Anders Perner³⁹, Colleen M. Plunkett²⁵, Marco Ranieri⁴⁰, Christa A. Schorr²², Maureen A. Seckel⁴¹, Christopher W. Seymour⁴², Lisa Shieh⁴³, Khalid A. Shukri⁴⁴, Steven Q. Simpson⁴⁵, Mervyn Singer⁴⁶, B. Taylor Thompson⁴⁷, Sean R. Townsend⁴⁸, Thomas Van der Poll⁴⁹, Jean-Louis Vincent⁵⁰, W. Joost Wiersinga⁴⁹, Janice L. Zimmerman⁵¹ and R. Phillip Dellinger²²

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2016 Sepsis Guidelines

- Obtain cultures before starting antibiotics
- Start broad-spectrum i.v. antibiotics within one hour
- Volume resuscitation with i.v. crystalloids > 30 mL/kg within the first 3 hours
 - Administration of balanced crystalloids has a favorable effect on the composite of death, new RRT, and persistent renal impairment
- Colloid fluids may also be given if large amounts of crystalloids are being used

Treatment of Septic Shock

- Initial target **MAP >65** mmHg in patients with septic shock requiring vasopressors
- **Norepinephrine** is the first choice vasopressor for septic shock
- Vasopressin or epinephrine may be added if necessary

Treatment of Septic Shock

- Hemodynamic/cardiac assessment may be necessary (echo, cardiac output monitoring) if clinical examination does not reveal the cause of the shock
- Hydrocortisone – stress dose may be used as a supplement to pressors
- Lactate measurement can be used to guide extent of resuscitation with the goal of returning to normal lactate levels.

Cardiogenic Shock

- Hypotension secondary to decreased cardiac output
- Must ensure that there is no hypovolemia and optimal cardiac perfusion
- May require **inotropic agent** to promote contraction e.g. dobutamine
- Mechanical support (LVAD, aortic balloon pump, etc.) for refractory cases

Stress Cardiomyopathy

- Catecholamine-induced cardiac injury
 - Takotsubo cardiomyopathy
- Dilation of cardiac apex, LV outflow obstruction
- Reversible, support until recovery

Hypovolemic Shock

Causes:

- Hemorrhage
- Fluid loss (gastric fluid, diarrhea, burns)
- Interstitial fluid accumulation (third spacing)

- **Volume resuscitation** with crystalloids
 - Whole blood may be considered in the case of significant anemia

Anemia and Transfusion

- Evaluate for active bleeding
 - GI: varices, ulcers, hemorrhoids, etc.
 - Procedure-related (retroperitoneal, hemothorax)
- Reversible causes
 - Check iron, vitamin B₁₂, folate levels
 - Marrow-suppressing medications
- **Transfuse packed rbc's for Hb<7 g/dL**
 - May consider whole blood for severe hypovolemic shock

NEJM 1999 Feb 11;340(6):409-17

COVID-19 Cardiac Involvement

- Mechanism of injury is unclear
- High troponin levels are associated with poor prognosis
- Current observations include:
 - Diffuse LV dysfunction
 - Cardiogenic shock related to cytokine storm
 - Fatal arrhythmias
 - Pericardiomyocarditis

Congestive Heart Failure

- Cardiac dysfunction resulting in reduced cardiac output and/or elevated intracardiac pressures
- May be from impairment of either systolic or diastolic function

Diastolic Failure

- During diastole, the atria of the heart contract, filling the ventricles
- Decreased cardiac compliance, impaired atrial contractility, or tricuspid/mitral valve stenosis may result in poor filling
- Heart becomes **pre-load dependent**
- Patients may benefit from **higher CVP** (8-12 mmHg) to optimize cardiac filling
 - May give fluids to increase filling pressures

Systolic Failure

- During systole, ventricular contraction pumps blood into the pulmonary artery and aorta
- Poor ventricular contraction, tricuspid/mitral valve regurgitation, pulmonic/aortic valve stenosis can result in poor ventricular output
- LV ejection fraction $\leq 40\%$

Systolic Failure

- Heart becomes **afterload sensitive**
- Patients may benefit from **afterload reduction**
 - Traditional diuretics (Loop diuretics)
 - ACE inhibitors
 - Direct vasodilators: hydralazine in combination with **nitrates** for patients with renal pathology
- Patients with hypotension may require positive inotropic agent +/- pressor

Tachycardia

- Sinus tachycardia
 - Common causes include hypovolemia/hypotension, hypoxia, PE, and pain
 - Address underlying condition
- Narrow Complex (QRS \leq 120ms)
 - Atrial fibrillation/flutter
 - Re-entrant tachycardia
- Wide Complex (QRS \geq 120ms)
 - Ventricular tachycardia until proven otherwise

Atrial Fibrillation

- Common cause of tachycardia in the ICU
- May have rapid ventricular response (HR>120)
- Look for exacerbating factors such as volume overload causing atrial stretching, hyperthyroidism, electrolyte abnormalities
- May cause hypotension as rapid heart rate can **decrease filling time** and subsequently stroke volume
- Initiate treatment to identify and control the precipitating factor then control HR

Acute Medical Treatment of RVR

- Selective β_1 antagonists
 - Metoprolol 5 mg i.v. over 1-2 minutes, may be repeated x2
- Calcium channel antagonist – like Diltiazem or Verapamil if LV systolic function is normal
- Patients may require drips of β -blocker or calcium channel blocker (see Appendix 1)
- Amiodarone drip for refractory RVR
- When SVT is suspected Adenosine can be used
 - Causes transient cardiac pause
 - 6 mg i.v. push. If no response repeat at 12 mg i.v. push.

Ventricular Tachycardia

- Sustained Monomorphic Ventricular Tachycardia
 - Unstable = Cardioversion and ACLS
 - Stable
 - ▶ Related to structural heart disease
 - Amiodarone then cardioversion if not terminated
 - ▶ Idiopathic
 - Verapamil if history of verapamil sensitive VT
 - β -blockers for outflow track VT
- Cardiology consult for further support

Acute Coronary Syndrome

Constellation of clinical symptoms compatible with acute myocardial ischemia

- ST-segment elevation MI (STEMI): coronary occlusion resulting in transmural ischemia
- non-ST-segment elevation MI (NSTEMI): Partial coronary obstruction resulting in subendocardial ischemia
- unstable angina: pain at rest or with minimal exertion, crescendo pattern

General Measures for MI

- Optimize oxygen delivery
- Obtain EKG, ensure electrolytes are within normal limits
- Decrease cardiac workload
 - β -blocker to decrease cardiac wall stress and heart rate
 - Make sure the patient is adequately resuscitated as decrease in heart rate may result in decreased cardiac output in the setting of hypovolemia
- Serial troponin levels
- Echocardiogram

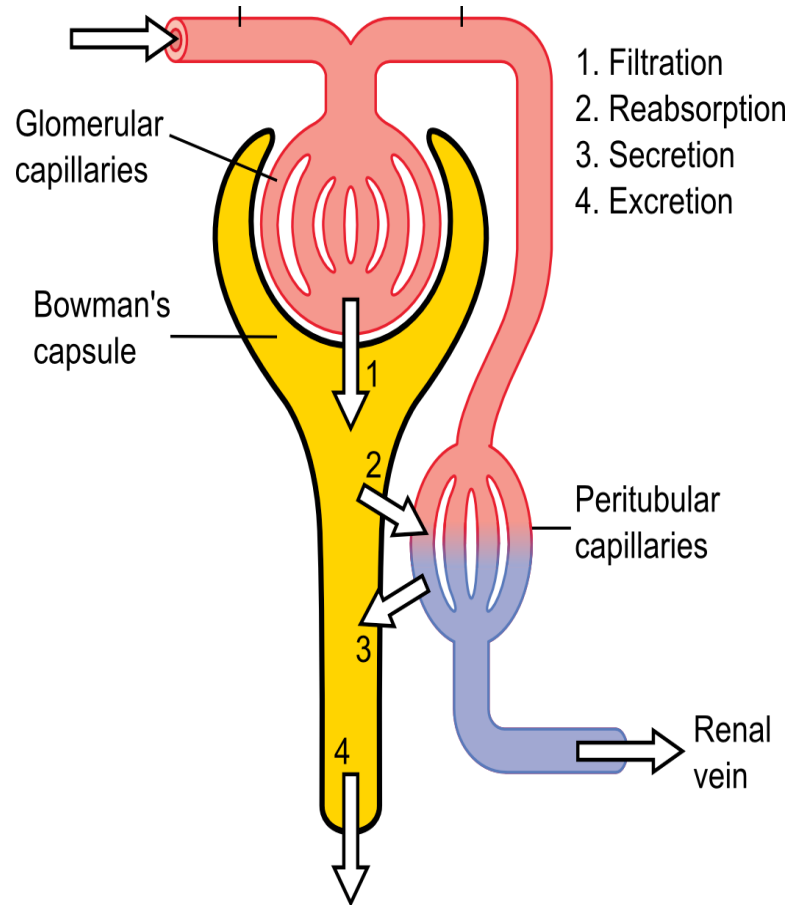
Treatment of STEMI

- Percutaneous coronary intervention
- Fibrinolytic therapy for cases where PCI cannot be performed in a timely fashion

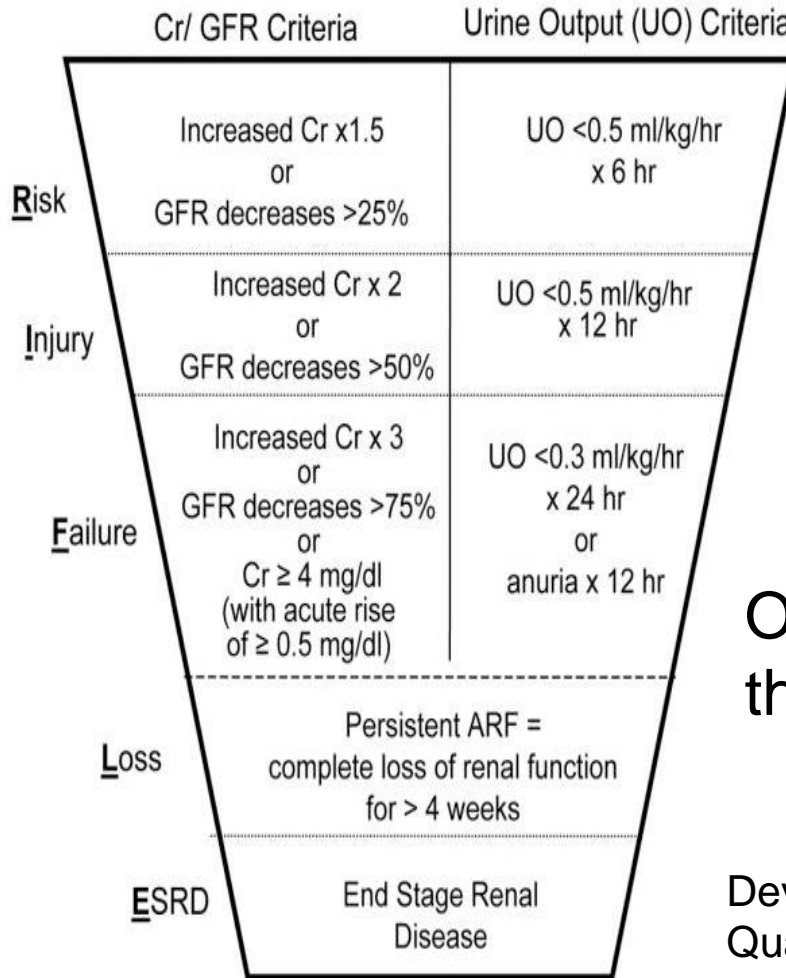
Treatment of NSTEMI/UA

- Antiplatelet therapy
 - aspirin
 - clopidogrel
 - glycoprotein 2b/3a inhibitors
- β -blockers, ACEIs, statins
- Avoid calcium channel blockers in the acute setting

Acute Kidney Injury and Renal Failure



RIFLE Criteria



Oliguria: urine output less than 0.5 ml/kg/hr

Developed by the Acute Dialysis Quality Initiative (ADQI)

Acute Kidney Injury Network (AKIN)

Stage	Serum Creatinine	Urine Output
1	1.5-1.9 times baseline OR ≥0.3 mg/dl increase	<0.5 ml/kg/hr for 6-12 hours
2	2.0-2.9 times baseline	<0.5 ml/kg/hr for ≥12 hours
3	3.0 times baseline OR Increase to ≥4.0 OR Initiation of renal replacement therapy	<0.3 mg/kg/hr for ≥24 hours OR Anuria for ≥12 hours

Kidney International Suppl 2012; 2(1)

Acute Kidney Injury Network (AKIN)

- Does not require known historical creatinine
- Only considered after adequate volume resuscitation
- Post-renal obstruction has been ruled out

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Pre-Renal AKI

Intravascular volume depletion

Decreased effective volume

- CHF
- Hypovolemia and dehydration
- Cirrhosis
- Early sepsis
- Renal vasoconstriction

Selective ischemia- renal artery stenosis

Diagnosis of Pre-Renal AKI

- Urine specific gravity > 1.020
- FeNa $< 1\%$
- Urine osmolarity > 350

Etiology of (intra-renal) AKD

and Typical* Urinalysis Findings

Acute Tubular Necrosis (ATN) [~ 90% of AKD cases]

- urine sediment benign, mild proteinuria/hematuria
- muddy-brown casts

Allergic Interstitial Nephritis

- urine eosinophils
- variable urine sediment, proteinuria and hematuria

Rhabdomyolysis

- brown urine, dip stick (+) blood but RBC (-) by microscopy
- myoglobin (+)

Glomerulonephritis

- marked proteinuria
- RBC casts (highly specific)

* urinalysis is often non-diagnostic

Acute Tubular Necrosis

Death of renal tubular cells

- Hypotension/hypoxia
- Rhabdomyolysis
- Cytotoxic drugs
- Aminoglycosides
- Blood transfusion reactions

Usually reversible if underlying cause is remedied

Prevention

- Maintain hydration (isotonic i.v. fluids)
- Reducing risk from nephrotoxins
 - Single vs. multiple daily doses of aminoglycosides
 - Lipid complex vs. standard amphotericin
 - Iso-osmotic vs. standard or “low” osmolality radiocontrast media
- Maintain perfusion pressure

Acute Kidney Injury

High Risk	1	2	3
	Discontinue all nephrotoxic agents when possible		
	Ensure volume status and perfusion pressure		
	Consider functional hemodynamic monitoring		
	Monitor Serum creatinine and urine output		
	Avoid hyperglycemia		
	Consider alternatives to radiocontrast procedures		
	Non-invasive diagnostic workup		
	Consider invasive diagnostic workup		
		Check for changes in drug dosing	
		Consider Renal Replacement Therapy	
		Consider ICU admission	
			Avoid subclavian catheters if possible

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Treatment of AKI

- Avoid or minimize exposure to nephrotoxic agents
- Diuretics only used to treat volume overload
 - Have no impact on recovery or prognosis
- Use crystalloids for volume expansion except in cases of hypovolemic shock
- Vasopressors may be used **in conjunction with fluid resuscitation** in cases of vasomotor shock
- Do not use low-dose dopamine

Indications For Dialysis

- Life-threatening conditions
 - Acute pulmonary edema from volume overload
 - Electrolyte Imbalance
 - Hyperkalemia
 - Hyponatremia
 - Increased calcium phosphate product
 - Uremia
 - Encephalopathy
 - Pericarditis
 - Intractable nausea and vomiting
 - Acidosis

Palliative Care

Ultimately, the goal of treatment is to facilitate a patient's recovery to **a condition that the patient would find acceptable.**

If this cannot be achieved, limitations of care should be discussed with the patient and the patient's family.

A provider may choose to withhold a therapy if it is believed to be futile in the care of the patient.

Palliative Care

Limitations of care may include (but are not limited to):

■ DNR Arrest

- Pursue all care unless patient suffers a cardiac arrest

■ DNI

- Do not intubate

■ DNR Comfort Care

- Withdraw supportive measures
- Patient's comfort becomes the highest priority

Palliative Care

May consider specific therapies individually:

- Dialysis
- Vasopressors
- Antibiotics
- Procedures
 - Tracheostomy
 - Percutaneous gastostomy/feeding tube
 - Vascular access

Palliative Care – ICU Triggers

- SNF patient with poor performance status
- Advanced dementia
- Age over 80 – all COVID +
- Age over 70 + 1 advanced organ system disease – ESRD, O₂-dependent COPD, Stage C/D CHF, Childs B/C cirrhosis
- Metastatic malignancy
- Advanced organ system disease
 - ESRD
 - O₂ dependent COPD
 - Advanced CHF
 - Child B/C cirrhosis
- Worsening clinical course on mechanical ventilation
- Shock state needing pressors for more than 2 days

The End

Remember:

Follow your local protocols

Stay safe and healthy

Special thanks to:

Berje Shammassian, M.D

Neurosurgery Training Program

University Hospitals of Cleveland/Case Western Reserve University

Appendix 1: Vasoactive Drugs

ADULT PATIENTS ONLY

Dosing and Titration Recommendations for Vasoactive Agents							
ALL titration endpoints need to be double-checked with the prescriber.							
Drug (infusion rate)	Concentration (EMR available concentrations listed)	Starting Dose	Upper Dosing Range	Bidirectional Titration Frequency	Bidirectional Titration Dose	Titration Endpoint/Goal	Alaris Min/Max
Clevidipine (mg/hr)	25mg/50mL Premix (fat emulsion)	1-2 mg/hr	1-21 mg/hr	1.5 min -10 min	≤ 50% hourly dose	MAP or SBP	1-16 mg/hr Hard Max: 32
Diltiazem (mg/hr)	125mg/125mL D5W/NS 250mg/250mL D5W/NS	Bolus ₁ : 0.25 mg/kg (Avg. 20 mg) Bolus ₂ : 0.35 mg/kg (Avg. 25 mg) Infusion: 5 mg/hr	10-15 mg/hr	2-5 min	5 mg/hr	HR between 80 to 100 bpm	1-15 mg/hr Hard Max: 20
Dobutamine (mcg/kg/min)	1000mg/250mL D5W Premix	2.5-5 mcg/kg/min	20 mcg/kg/min	5-10 min	2.5 mcg/kg/min	CI ≥ 2.5 L/min/m ² or MAP	0.5-20 mcg/kg/min Hard Max: 40
Dopamine ^V (mcg/kg/min)	400mg/250mL ^P D5W Premix 800mg/250mL ^C D5W/NS	5 mcg/kg/min	>20 mcg/kg/min not beneficial	2-5 min	0.5-2.5 mcg/kg/min	MAP between 60 and 70 mmHg	0.5-20 mcg/kg/min
Epinephrine ^V (mcg/kg/min)	4mg/250mL ^C D5W/NS 10mg/250mL ^C D5W/NS	0.01-0.05 mcg/kg/min	0.5-1 mcg/kg/min	1-5 min	0.01-0.05 mcg/kg/min	MAP between 60 and 70 mmHg	0.01-1 mcg/kg/min
	Peripheral administration: 4mg/250mL at a MAX rate of 0.2 mcg/kg/min for MAX of 8 hours						
Esmolol ^V (mcg/kg/min)	2500mg/250mL NS 2000mg/100mL NS (premixed)	Bolus ₁ : 500 mcg/kg Infusion: 50 mcg/kg/min	200-300 mcg/kg/min	4 min	50 mcg/kg/min	HR between 80 to 100 bpm	50-300 mcg/kg/min
Isoproterenol (mcg/kg/min)	1mg/250mL D5W	0.01 mcg/kg/min	0.01-0.2 mcg/kg/min	1-2 min	0.01 mcg/kg/min	HR between 60 and 80	0.01-0.09 mcg/kg/min Hard Max: 0.2
Labetalol (mg/min)	300mg/300mL D5W/NS 500mg/100mL(undiluted)	Bolus ₁ : 10-20 mg Infusion: 0.5-2 mg/min (0.1 mg/min after 300 mg infused)	6-8 mg/min	5-15 min	0.5-1 mg/min	MAP or SBP	1-6 mg/min Hard Max: 8

Appendix 1: Vasoactive Drugs

ADULT PATIENTS ONLY

Drug (infusion rate)	Concentration (EMR available concentrations listed)	Starting Dose	Upper Dosing Range	Bidirectional Titration Frequency	Bidirectional Titration Dose	Titration Endpoint/Goal	Alaris Min/Max
Milrinone (mcg/kg/min)	20mg/100mL D5W Premix	0.1 (Heart Failure) - 0.375 mcg/kg/min	0.5-0.75 mcg/kg/min	2 hours	0.1 mcg/kg/min	CI \geq 2.5 L/min/m ² or MAP	0.15-0.75 mcg/kg/min Hard Max: 0.75
Nitroprusside (mcg/kg/min)	50mg/100mL NS Premix	0.25-0.5 mcg/kg/min	3-5 (Max 5mcg/kg/min for 10 min., if BP not controlled switch agents)	3-5 min	0.5 mcg/kg/min	MAP or SBP	0.1-3 mcg/kg/min Hard Max: 5
Norepinephrine ^v (mcg/kg/min)	8mg/250mL ^C 16mg/250mL ^C D5W/NS	0.01-0.05 mcg/kg/min	0.5-1 mcg/kg/min Add VP around 0.2; > 0.5 mcg/kg/min not recommended	1-5 min	0.01-0.05 mcg/kg/min	MAP between 60 and 70 mmHg	0.01-3 mcg/kg/min Hard Max: 3.3
	Peripheral administration: 8mg/250mL at a MAX rate of 0.2 mcg/kg/min for MAX of 8 hours						
Phenylephrine ^v (mcg/kg/min)	10mg/250mL ^P 80mg/250mL ^C D5W/NS	0.5-1 mcg/kg/min	2 mcg/kg/min (Standard conc.) 9 mcg/kg/min (High conc.)	1-5 min	0.5 mcg/kg/min	MAP between 60 and 70 mmHg	0.1-4 mcg/kg/min Hard max: 9.1
	Peripheral administration: MAX rate of 0.03 units/min for MAX of 8 hours						
Vasopressin ^v (units/min)	20units/100mL ^C D5W/NS	0.03 units/min	0.03 units/min	Titration per provider request in certain patient populations		MAP between 60 and 70 mmHg	0.01-0.06 units/min Hard max: 0.1
	Peripheral administration: MAX rate of 0.03 units/min for MAX of 8 hours						
Nicardipine (mg/hr)	40mg/200mL ^P NS Premix	2.5-5 mg/hr	10-15 mg/hr	5-15 min	2.5-5 mg/hr	MAP or SBP	0.5-15 mg/hr
Nitroglycerin (mcg/min)	50mg/250mL D5W Use PVC Free tubing	5 mcg/min	200 mcg/min	3-5 min	5-10 mcg/min	MAP or SBP or chest pain relief	1-200 mcg/min

^v = "vesicant", ^P = "peripheral line", ^C = "central line"

Appendix 2: Sedative Drugs

ADULT PATIENTS ONLY

Dosing and Titration Recommendations for Analgesia, Sedation and Paralysis

ALL titration endpoints need to be double-checked with the prescriber

Drug (infusion rate)	Concentration (EMR available concentrations listed)	Starting Dose	Upper Dosing Range	Bidirectional Titration Frequency	Bidirectional Titration Dose	Titration Endpoint/Goal	Alaris Min/Max
Fentanyl (mcg/hr) <small>*use Sedation Algorithm</small>	1000 mcg/100mL NS 2500 mcg/250mL NS	Bolus: 25-50 mcg Infusion: 25 mcg/hr	200-300 mcg/hr	30 min	25 mcg/hr	RASS of 0 to -2 and/or CPOT	10-300 mcg/hr [†]
Propofol (mcg/kg/min) <small>*use Sedation Algorithm</small>	1000 mg/100mL Premix (fat emulsion)	5 mcg/kg/min	50-100 mcg/kg/min	5 min	5 mcg/kg/min	RASS of 0 to -2	5-50 mcg/kg/min Hard max: 600
Midazolam (mg/hr) <small>*use Sedation Algorithm</small>	100 mg/100mL D5W/NS	Bolus: 2-4 mg Infusion: 2 mg/hr	15-20 mg/hr	30 min – 1hr	25%	RASS of 0 to -2	0.5-20 mg/hr [†]
Dexmedetomidine (mcg/kg/hr) <small>*use Sedation Algorithm</small>	400 mcg/100mL NS Premix	0.2 mcg/kg/hr	1-1.4 mcg/kg/hr	30 min	25%	RASS of 0 to -2	0.1-1.4 mcg/kg/hr Hard max: 2.5
Lorazepam (mg/hr) <small>*use Sedation Algorithm</small>	50 mg/50mL D5W	Bolus: 2-4 mg Infusion: 1 mg/hr	5-10 mg/hr	30 min – 1 hr	25%	RASS of 0 to -2	0.5-10 mg/hr
Ketamine [‡] (mg/kg/hr) <small>Doses vary highly based on indication</small>	500mg/250 mL NS	Bolus: 0.1 mg/kg Infusion: 0.05 mg/kg/hr	1-2 mg/kg/hr	15 min	25%	RASS of 0 to -2	0.05-6 mg/kg/hr
Morphine (mg/hr) <small>*End of Life ONLY, use Withdrawal of LST Algorithm or End of Life Ordersets</small>	100 mg/100mL NS	Bolus: 2-4 mg Infusion: 2 mg/hr	20-30 mg/hr	15-30 min	1 mg/hr	RDOS < 3*	0.5-10 mg/hr
Cisatracurium (mcg/kg/min) <small>*use Paralysis Algorithm</small>	200 mg/100mL D5W/NS	Bolus: 0.1 mg/kg Infusion: 3 mcg/kg/min	7.5-10 mcg/kg/min	30 min- 1 hr	25%	TOF 2-3 out of 4	0.5-10 mcg/kg/min Hard max: 10
Rocuronium (mcg/kg/min) <small>*use Paralysis Algorithm</small>	1000/250mL D5W/NS	Bolus: 0.6 mg/kg Infusion: 8 mcg/kg/min	12 mcg/kg/min	30 min-1 hr	25%	TOF 2-3 out of 4	1-12 mcg/kg/min

[†] = High concentration drips available for patients with high dose requirements, call local pharmacy for assistance



* Respiratory Distress Observation Scale [‡] Separate dosing regimens available for Chronic Pain and Status Epilepticus, Depression and Migraine.

Appendix 3: Surviving Sepsis Campaign: Guidelines for the Management of COVID-19

I. Infection Control

- For aerosol-generating procedures, use fitted respirator masks (N95 respirators, FFP2, or equivalent) (best practice).
- Perform aerosol-generating procedures in negative pressure room (best practice).
- For usual care for non-ventilated patients, use surgical/medical masks (weak recommendation).
- For non-aerosol-generating procedures on ventilated patients, use surgical/medical masks (weak recommendation).
- For intubation, use video-guided laryngoscopy over direct laryngoscopy (weak recommendation).
- Intubation should be performed by provider most experienced with airway management (best practice).

II. Laboratory Diagnosis and Specimens

- For intubated and mechanically ventilated adults:
 - Obtain lower respiratory tract over nasopharyngeal/oropharyngeal samples (weak recommendation).
 - Obtain endotracheal aspirates over bronchial wash/bronchoalveolar lavage samples (weak recommendation).

Appendix 3: Surviving Sepsis Campaign: Guidelines for the Management of COVID-19

III. Supportive Care

- Use dynamic parameters, skin temperature, capillary refilling time, and/or serum lactate over static parameters to assess fluid responsiveness (weak recommendation).
- Use conservative over liberal fluid strategy (weak recommendation).
- Use crystalloids over colloids (strong recommendation).
- Use buffered/balanced crystalloids over unbalanced crystalloids (weak recommendation).
- Do not use hydroxyethyl starches (strong recommendation).
- Do not use gelatins (weak recommendation).
- Do not use dextrans (weak recommendation).
- Do not routinely use albumin for initial resuscitation (weak recommendation).
- Use norepinephrine as first-line vasoactive agent (weak recommendation).
- If norepinephrine not available, use vasopressin or epinephrine (weak recommendation).
- Do not use dopamine if norepinephrine is available (strong recommendation).
- Add vasopressin as second-line agent if target MAP can't be achieved by norepinephrine alone (weak recommendation).
- Titrate vasoactive agents to target MAP of 60-65 mmHg (weak recommendation).
- For cardiac dysfunction and persistent hypoperfusion despite fluid resuscitation and norepinephrine, add dobutamine (weak recommendation).
- For refractory shock, use low-dose corticosteroid therapy (weak recommendation).
- Start supplemental O₂ if SPO₂ is < 92% (weak recommendation) and if SPO₂ is < 90% (strong recommendation).

Appendix 3: Surviving Sepsis Campaign: Guidelines for the Management of COVID-19

- Maintain SPO2 no higher than 96% (strong recommendation).
- For acute hypoxemic respiratory failure despite conventional O2 therapy, use HFNC (weak recommendation).
- In acute hypoxemic respiratory failure, used HFNC over NIPPV (weak recommendation).
- If HFNC not available and no urgent indication for intubation, trial NIPPV with close monitoring (weak recommendation).
- No recommendation regarding use of helmet NIPPV compared with mask NIPPV.
- Recommend close monitoring for worsening of respiratory status (best practice).
- Use low tidal volume ventilation (Vt 4-8 mL/kg) (strong recommendation).
- Target plateau pressures (Pplat) of < 30 cm H2O (strong recommendation).
- For moderate to severe ARDS, use higher PEEP strategy (weak recommendation).
- For ARDS, use conservative fluid strategy (weak recommendation).
- For moderate to severe ARDS, use prone ventilation for 12 to 16 hours (weak recommendation).
- For moderate to severe ARDS:
 - Use intermittent boluses of neuromuscular blocking agents over continuous infusion (weak recommendation).
 - If persistent ventilator dyssynchrony, use continuous NMBA infusion for up to 48 hours (weak recommendation).
- Do not routinely use inhaled nitric oxide (strong recommendation).
- In severe ARDS and hypoxemia, trial inhaled pulmonary vasodilator; if no rapid improvement, treatment should be tapered off (weak recommendation).
- For hypoxemia despite optimizing ventilation, use recruitment maneuvers (weak recommendation).
- For recruitment, do not use staircase (incremental PEEP) recruitment maneuvers (strong recommendation).
- In refractory hypoxemia despite optimizing ventilation, rescue therapies, and proning, use venovenous ECMO (weak recommendation).

Appendix 3: Surviving Sepsis Campaign: Guidelines for the Management of COVID-19

IV. COVID-19 Therapy

- In respiratory failure (without ARDS), do not routinely use systemic corticosteroids (weak recommendation).
- In ARDS, use systemic corticosteroids (weak recommendation).
- In respiratory failure, use empiric antimicrobials/antibacterial agents (weak recommendation).
- For fever, use acetaminophen for temperature control (weak recommendation).
- Do not routinely use IVIG (weak recommendation).
- Do not routinely use convalescent plasma (weak recommendation).
- In critically ill adults:
 - Do not routinely use lopinavir/ritonavir (weak recommendation).
 - Insufficient evidence on the use of other antiviral agents.
- Insufficient evidence on the use of recombinant rIFNs.
- Insufficient evidence on the use of chloroquine or hydroxychloroquine.
- Insufficient evidence on the use of tocilizumab.