

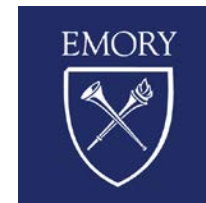
Management of Severe COVID

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Objectives

- Review context of pandemic outcomes and the literature
 - Basic inpatient management of severe COVID
 - Management of critically ill COVID patient
 - ECMO utilization and outcomes
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- The bottom of the slide features a decorative graphic consisting of several overlapping, semi-transparent geometric shapes. On the left, there is a large blue triangle pointing downwards. In the center, there is a purple triangle pointing upwards. On the right, there is a light blue triangle pointing downwards. These shapes overlap to create a modern, abstract design.

Definitions

- Severe disease, at least one of*:
 - Dyspnea
 - RR > 30
 - SpO₂ < 94% on room air
 - P:F < 300
 - Infiltrates in more than 50% of lung field
- Critical illness:
 - Requiring advanced oxygen therapy
 - HFNC, NRB, HHFNC, CPAP, NIPPV, mechanical ventilation, ECMO
 - Other organ failure
- Significant variations in definitions in literature

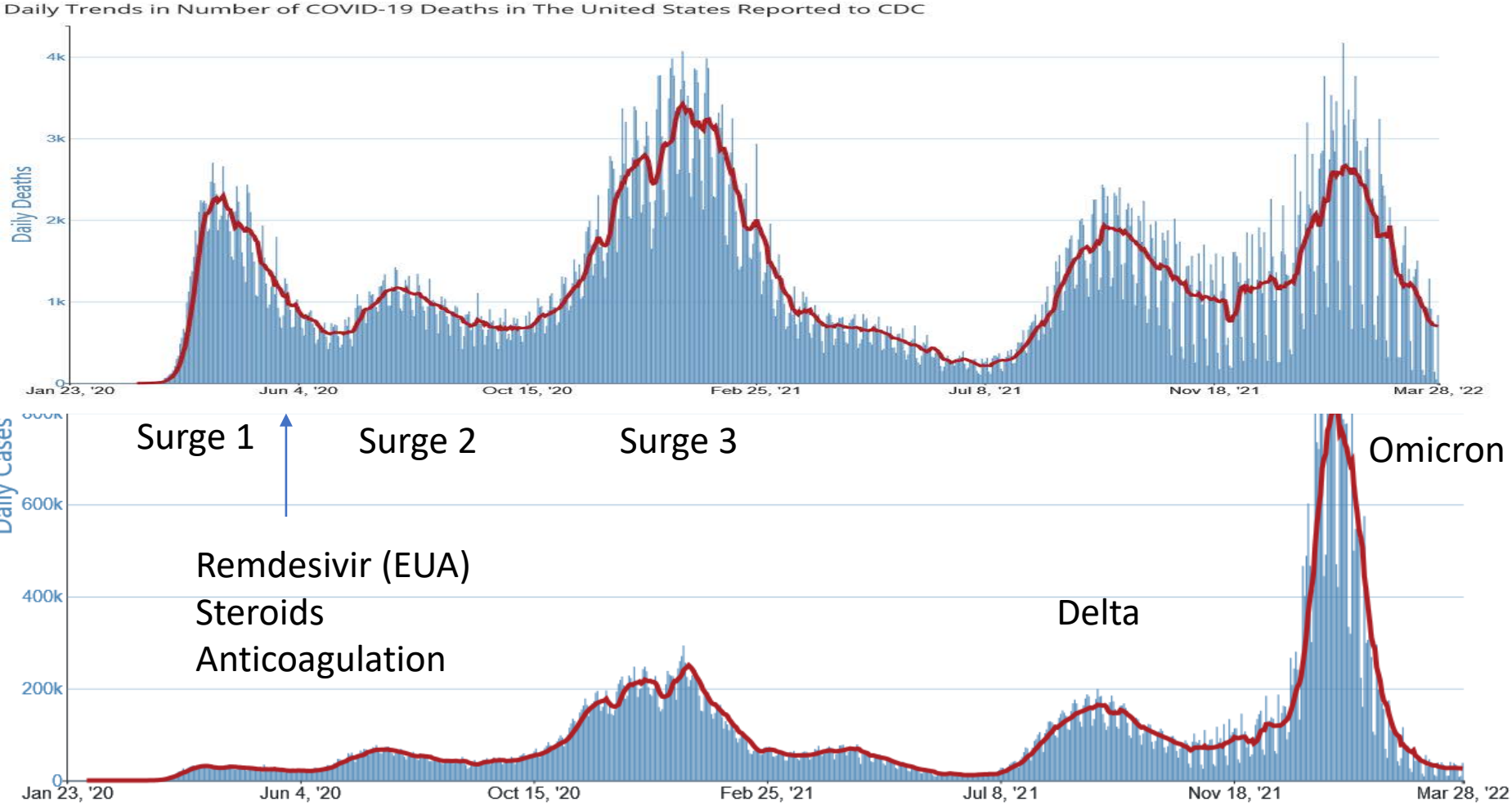
* Berlin et al. Severe COVID-19. *N Engl J Med* 2020;383:2451-60.

Outcome variance

- Difficulty generalizing against changes in:
 - Variants
 - Testing rates
 - Data collection
 - Immunization rates
 - Therapeutics
 - System stresses
 - Population selection

Daily cases versus deaths

https://covid.cdc.gov/covid-data-tracker/#trends_dailycases




Literature Gold Rush


- Pubmed basic search as of 5/25/22
- Includes some studies where referenced but not study subject
- Be very careful with the literature

	“COVID” (2019-2022)	“INFLUENZA” (1892-2022)
All	256,375	148,127
Controlled trials	1,459	3,955
Controlled, multicenter trials	331	847
Observational study	4,761	767
All trials	10,009	7,518
Reviews and Meta-analyses	32,111	14,822
Editorials	11,238	2,104
Case reports	13,480	5,807
Errors and retractions	1860	363

Severe management (Minimal O2 support)


- Pre-critical illness
 - Supplemental oxygen
 - Self-proning, vitamins, micronutrients (no data)
 - Steroids (RECOVERY)
 - Remdesivir (ACTT-1)
 - Other therapeutics discussed next
 - >6L NC prompts transfer to ICU
 - Standard VTE prophylaxis
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Critical Illness

- Moderate to severe respiratory failure
 - Inflammatory response
 - Hypercoagulable state
 - Secondary infections
 - Other organ failure
 - Organizing pneumonia
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Outline

- Therapeutics (separate presentation)
 - Unclear and impractical: PLEX, radiation
 - Ruled out: Convalescent plasma, host of therapeutics, HCQ, Ivermectin, stem cells

 - Advanced O2 delivery
 - Steroids
 - Anticoagulation
 - ECMO
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To intubate or not to intubate

- Persistent fear of intubation
- No difference in outcome with initial mode *
 - HHFNC, NIPPV, Ventilator
- Observational studies with selection bias
 - No RCT for intubation criteria, never will be
- Anecdotally worse ECMO outcomes if prolonged pre-intubation BiPAP

* Hernandez-Romieu AC et al. Timing of Intubation and Mortality Among Critically Ill Coronavirus Disease 2019 Patients: A Single-Center Cohort Study. *Critical Care Medicine*, 01 Nov 2020, 48(11):e1045-e1053

Moderate to severe respiratory failure

- Standard ARDS management
 - Lung protective ventilation
 - Proning, paralysis, inhaled pulmonary vasodilators

Steroids

- RECOVERY: 29% vs 41% mortality on vent, 23% vs 26% non-ventilated
 - JAMA meta-analysis similar findings
 - Dexamethasone
 - 6mg/day x5-10 days
 - Only if on oxygen therapy
 - Bulk of studied patients not critically ill
- Intermediate and higher dose regimens not yet rigorously studied
 - Likely some role
 - Organizing pneumonia
 - Optimal dose, timing and duration unknown

* NEJM July 2020 “Dexamethasone in Hospitalized Patients with Covid-19 — Preliminary Report”

** JAMA Sept 2, 2020 “Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis”

Steroids

- Organizing pneumonia

- Findings ascribed to fibrosis may be organizing pneumonia

- Interstitial inflammation
 - Diffuse ground glass to dense consolidations
 - CT needed to assess
 - Often normal looking lungs months after recovery

- Can occur even after initial recovery

- Treatment

- High dose steroid (2mg/kg/day methylprednisolone) with prolonged taper over many weeks

Anticoagulation

- INSPIRATION trial
 - 562 patients, 10 hospitals in Iran
 - Lovenox 1mg/kg/day (intermediate) vs 40mg/day (prophylactic): no difference
 - Extremely low APACHE-II scores
- RAPID trial
 - 465 patients, 28 hospitals in Brazil, Canada, Ireland, Saudi Arabia, United Arab Emirates, and US
 - High-standard heparin or equivalent Lovenox vs prophylactic dose
 - No difference in composite, but 78% reduction in all-cause mortality
 - No difference in critically ill subgroup

Anticoagulation

- Clearly some discrepancies
- EUH consensus: internal data do not show harm, marked reduction in thrombotic complications including PE/DVT
 - Tier 1: Prophylactic dosing (floor)
 - Tier 2: Critically ill (provider discretion)
 - Tier 3: Evidence of thrombosis

INSPIRATION Investigators, Effect of Intermediate-Dose vs Standard-Dose Prophylactic Anticoagulation on Thrombotic Events, Extracorporeal Membrane Oxygenation Treatment, or Mortality Among Patients With COVID-19 Admitted to the Intensive Care Unit: The INSPIRATION Randomized Clinical Trial. JAMA. 2021;325(16):1620-1630. (March)


Sholzberg et al. Effectiveness of therapeutic heparin versus prophylactic heparin on death, mechanical ventilation, or intensive care unit admission in moderately ill patients with covid-19 admitted to hospital: RAPID randomised clinical trial. BMJ. 2021 Oct 14;375:n2400.

ECMO

Extracorporeal membrane oxygenation support in COVID-19: an international cohort study of the Extracorporeal Life Support Organization registry

Barbaro et al. *Lancet*. 2020 Oct 10;396(10257):1071-1078.

- 1035 patients with COVID from Jan 16 to May 1, 2020
 - 213 hospitals in 36 countries

 - 39% mortality with final dispo to death or hospital discharge
 - Median duration of intubation to ECMO 4.0 days
 - 59% received any form of non-invasive ventilation
 - Only < 32% (ambiguous) received any BiPAP/CPAP
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ECMO

Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry

Barbaro et al. *Lancet*. 2021 Oct 2;398(10307):1230-1238.

- 4812 patients with COVID from Jan 16 to Dec 31, **2020**
- 349 hospitals in 41 countries
- 50% mortality (up from 39%)
- 3 Groups
 - A1 – Early adopting centers from Jan 16 to May 1 (prior pub)
 - A2 – Early adopting centers from May 1 to Dec 31
 - B – Late adopting centers from May 1 to Dec 31
- Early adopting centers with better mortality

Mortality with ECMO pre and post COVID era

	2018	2019	2020 (COVID)
Viral Mortality	42%	29%	52%
Viral Run Length (days)	9.3	16.6	29.2
Bacterial Mortality	35%	38%	47%
Bacterial Run Length (days)	12.3	11.0	15.0

Source: North American Regional Trend Summary, ELSO Registry, October 2021

March 24, 2020

- Best therapy is good critical care



Clinical and team management in the
COVID-ICU:
Successful strategies from the first week

COVID-19 CLINICAL ROUNDS
Mark Caridi-Scheible, MD



Our approach

1. Need to deliver great critical care with high level of attention to detail and accountability
2. No luxury of time, get them better FAST for:
 - Sake of patient's chance of recovery
 - Sake of the next patient that will need that ventilator
3. Procedures should be pre-emptive
 - unpredictable and rapid declines
 - Constraints and delays of PPE and provider safety

References

- Berlin et al. Severe COVID-19. *N Engl J Med* 2020;383:2451-60.
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- North American Regional Trend Summary, ELSO Registry, October 2021. Available at <http://www.elseo.org>.