Emergency Use of the Hemolung Device

**DESCRIPTION:**
As we are preparing for a potential surge in ICU patients as COVID-19 penetrates the community, it is our hope that extracorporeal carbon dioxide removal (ECCO2R) could be used in any hypercapnic respiratory failure syndrome and in patients with acute respiratory distress syndrome (ARDS) to facilitate instituting lung protective ventilation.

**CONSIDERATION TO USE ECCO2R MAY BE:**
- pH <7.20 from hypercapnia, and/or
- Plateau pressure >30 cm H2O or driving pressure >15 cm H2) despite optimization of mechanical ventilation.
MHIF Research Shared at Virtual ACC 2020

50 Total Presentations
• 32 Poster board Abstracts
• 7 Moderated or Oral Abstracts
• 11 Talks and Podium Presentations

66 MHIF/MHI Physician, Fellows, & Staff
• 31 MHI Physicians
• 5 Clinical Fellows and Residents
• 13 MHIF Staff Members
• 8 International Scholars
• 7 MHIF Interns
• 2 Allina Staff Members
A Perspective on the Chinese Experience with COVID-19

Yu Du, M.D.
Minneapolis Heart Institute Foundation, Abbott Northwestern Hospital
Dept. of Cardiology, Beijing Anzhen Hospital, Capital Medical University

Disclosures

• For educational and reference purposes only

• Recommendations on COVID-19 Management mainly on a basis of
  Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (7th edition)
  published by China National Health Commission on March 4, 2020
Outline

• What is the coronavirus disease 2019 (COVID-19)?
• How to prevent & identify COVID-19 infection?
• How to control COVID-19 pandemic?
• How to manage patients with COVID-19?
• COVID-19 & Cardiovascular Disease

COVID-19: SARS-CoV-2

• A cluster of cases of pneumonia with unknown etiology in Wuhan, China
• SARS-CoV-2, a novel coronavirus, leading to coronavirus disease 2019 (COVID-19)
• Coronavirus β genus, shares 96% homology with SARS-like coronavirus strain (BatCov RaTG13)
COVID-19: SARS-CoV-2

- Medium-sized enveloped positive-stranded RNA virus
- Crown-like particles observed under transmission electron microscope (TEM)
- Origin: most probably from natural selection
- Fragile to ultraviolet and heat (56 °C for 30 min)

Inactivated by liposoluble solvents

SARS, severe acute respiratory syndrome
MERS, Middle East respiratory syndrome
Andersen, K.G. et al. Nat Med (2020)

COVID-19: Geographic Distribution
by April-6-2020 17:37

https://coronavirus.jhu.edu/map.html
COVID-19: Epidemiology

• Source of infection
  Infected patients (symptomatic or asymptomatic)

• Route of transmission
  Respiratory droplets and close contact
  Aerosol transmission: plausible (high concentration, closed environment, & long time)
  Fecal-oral transmission (virus detected: saliva, urine & stool)

• Susceptible population
  Human beings are generally susceptible !!!

COVID-19: Clinical Manifestation

• Incubation period: 1-14 days following exposure (predominately 4~5 days)

• Common symptoms: fever (44% on admission [36.7-38.0 °C], 89% during hospitalization [37.8-38.9 °C]), dry cough & fatigue

• Clinical classification
  No/Mild/moderate (81%): no or mild pneumonia
  Severe (14%): dyspnea, hypoxemia, >50% lung involvement within 1~2 days
  Critical severe (5%): respiratory failure, shock, multi-organ dysfunction

• Prognosis: generally good, elderly and those with chronic comorbidities are relatively worse
  case fatality rate ranges from 5.8% (Wuhan) ~ 0.7% (rest of China), overall 2.3%

COVID-19: Differential diagnosis

- COVID-19 mild type
  Upper respiratory tract infections by other virus
- COVID-19 pneumonia
  Other known viral or mycoplasma pneumonia infections
- Other non-infectious disease
  eg. vasculitis, dermatomyositis, & organizing pneumonia

Nucleic acid test recommend:
Suspected cases, even common respiratory pathogen tested positive (co-infection)

COVID-19: Asymptomatic Infection Matters

Contagion tested positive

<table>
<thead>
<tr>
<th>Days</th>
<th>Consistent asymptomatic</th>
<th>Asymptomatic within incubation period</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>No symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Symptoms present</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

CT imaging findings
50% (12/24) had patchy/ground-glass opacities
20% (5/24) had atypical imaging


Viral Shedding
Viral load detected in asymptomatic patients, similar to that in symptomatic patients

COVID-19: Autopsy

85 y/o, male, died of COVID-19 & pulmonary failure, autopsy <12 hrs

1. Pleural thickening, adhesion (R)
2. White patchy lesion (L)
3. White viscous fluid overflow, fiberbands
4. White foam mucus in the trachea
5. Gelatinous mucus attachment in the R lung bronchus
6. Yellow clear liquid in the pericardial cavity
7. Myocardial section is gray red fishlike
8. Segmental dilatation & stenosis of small intestine alternate


COVID-19: Pathology

- Fig. A, B: bilateral diffuse alveolar damage with cellular fibromyxoid exudates, interstitial mononuclear inflammatory infiltrates (lymphocytes)
- Fig. A: desquamation of pneumocytes and hyaline membrane formation (ARDS)
- Fig. C: microvesicular steatosis
- Fig. D: interstitial mononuclear inflammation


ARDS, adult respiratory distress syndrome
COVID-19: Lab-routine Examination

- **Early stage**: leukocytes - / ↓, lymphocyte ↓
- **Most patients**: CRP ↑, ESR ↑, Procalcitonin -
- **Severe patients**: D-dimer ↑↑, lymphocyte ↓↓↓, inflammatory biomarkers ↑, troponins ↑

### Warning signs for disease progression
1) Lymphocytes ↓↓↓
2) Inflammatory markers ↑↑ (CRP, IL-6)
3) Lactic acid ↑↑
4) Pulmonary lesion on chest imaging ↑↑

COVID-19: Lab-etiological & serological Examination

<table>
<thead>
<tr>
<th></th>
<th>Etiological examination</th>
<th>Serological examination</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Target</strong></td>
<td>Viral nucleic acid</td>
<td>Specific IgM/IgG antibody against virus</td>
</tr>
<tr>
<td><strong>Mechanism</strong></td>
<td>RT-PCR &amp; NGS</td>
<td>GICA, ELISA, CLIA</td>
</tr>
<tr>
<td><strong>Specimen</strong></td>
<td>Upper airway (nasopharyngeal swab specimen)</td>
<td>Serum</td>
</tr>
<tr>
<td></td>
<td>Lower airway (sputum)</td>
<td></td>
</tr>
<tr>
<td><strong>Suggestion</strong></td>
<td>Continual test if negative at the beginning</td>
<td>Suspected cases with negative nucleic acid</td>
</tr>
</tbody>
</table>

RT-PCR, real-time polymerase chain reaction
COVID-19: Lab-etiological & serological Examination

Viral nucleic acid test

<table>
<thead>
<tr>
<th>Test results</th>
<th>Clinical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ - -</td>
<td>Patient may be in the window period of infection.</td>
</tr>
<tr>
<td>+ + -</td>
<td>Patient may be in the early stage of infection.</td>
</tr>
<tr>
<td>+ + +</td>
<td>Patient is in the active phase of infection.</td>
</tr>
<tr>
<td>+ - +</td>
<td>Patient may be in the late or recurrent stage of infection.</td>
</tr>
<tr>
<td>- + -</td>
<td>Patient may be in the early stage of infection. PCR result may be false-negative.</td>
</tr>
<tr>
<td>- - +</td>
<td>Patient may have had a past infection, and has recovered.</td>
</tr>
<tr>
<td>- + +</td>
<td>Patient may be in the recovery stage of an infection, or the PCR result may be false-negative.</td>
</tr>
</tbody>
</table>

PCR, polymerase chain reaction

https://www.biopanda.co.uk/

COVID-19: Chest CT Imaging

- (A) 56 y/o man: focal ground-glass opacity associated with smooth interlobular and intralobular septal thickening in the right lower lobes
- (B) 74 y/o woman: bilateral, peripheral ground-glass opacity associated with smooth interlobular and intralobular septal thickening (crazy-paving pattern).
- (C) 61 y/o woman: bilateral and peripheral predominant consolidation pattern with a round cystic change internally (arrow)
- (D) 63 y/o woman: bilateral, peripheral mixed pattern associated with air bronchograms in both lower and upper lobes, with a small amount of pleural effusion (arrows)

COVID-19: Chest CT & Viral Nucleic Acid

- Based on positive RT-PCR, chest CT sensitivity: 97%
- Based on positive RT-PCR, chest CT specificity: 25%
- 60%~93% pts. had initial positive CT consistent with COVID-19 prior (or parallel) to the initial positive RT-PCR
  

- Chest CT abnormalities identified in patients prior to the development of symptoms
  

CT imaging is very useful for COVID-19 clinical diagnosis, esp. in epidemic area (high sensitivity, easy access & rapid knowing results)

Classic CT imaging & symptom, even negative RT-PCR: Isolation and continuous RT-PCRs

Outline

- What is the coronavirus disease 2019 (COVID-19)?
- How to prevent & identify COVID-19 infection?
- How to control COVID-19 pandemic?
- How to manage patients with COVID-19?
- COVID-19 & Cardiovascular Disease
COVID-19: Basic Protective Measures

Stay home as much as possible

CDC (US): How to Protect Yourself & Others, updated April 4, 2020

Cover your mouth and nose with a cloth face cover when around others

COVID-19: Protections When Caring for Suspected/Confirmed Cases

For caregivers

- Ensure the ill person rests, drinks plenty of fluids and eats nutritious food.
- Wear a medical mask when in the same room with an ill person. Do not touch the mask or face during use and discard it afterward.

- Frequently clean hands with soap and water or alcohol-based rub, especially:
  - after any type of contact with the ill person or their surroundings
  - before, during and after preparing food
  - before eating
  - after using the toilet
- Use dedicated dishes, cups, eating utensils, towels and bedlinens for the ill person. Wash dishes, cups, eating utensils, towels, or bedlinens used by the ill person with soap and water.

- Identify frequently touched surfaces by the ill person and clean and disinfect them daily.
- Call your health care facility immediately if the ill person worsens or experiences difficulty breathing.
COVID-19: Other Protective Measures in China

Disinfection in public places

Temperature check

Wearing mask in public places

Prevention propagation

Fangcang Hosp.

Mutual help based on community

COVID-19: Personal Protection Equipment (health worker)

<table>
<thead>
<tr>
<th>Protection Level</th>
<th>Protective Equipment</th>
<th>Scope of Application</th>
</tr>
</thead>
</table>
| Level I protection | • Disposable surgical cap  
|                     | • Disposable surgical mask  
|                     | • Work uniform  
|                     | • Disposable latex gloves  
|                     | • Surgical mask (N95)  
|                     | • Lower respiratory protection device or powered air-purifying respirator  
|                   | All staff at the healthcare facilities  
|                     | Fever outpatient department  
|                     | Isolation ward area (including isolated intensive ICU)  
|                     | Naso-sinusosal or respiratory tract lavage  
|                     | Naso-respiratory specimen examination of suspected/confirmed patients  
|                     | Imaging examination of suspected/confirmed patients  
|                     | Cleaning of surgical instruments used with suspected/confirmed patients  |
| Level II protection | • Disposable surgical cap  
|                    | • Medical protective mask (N95)  
|                    | • Work uniform  
|                    | • Disposable medical protective uniform  
|                    | • Disposable latex gloves  
|                    | • Medical protective mask (N95)  
|                    | • Work uniform  
|                    | • Disposable medical protective uniform  
|                    | • Disposable latex gloves  
|                    | • Full face respiratory protection device or powered air-purifying respirator  
|                    | Staff in Emergency dept., outpatient dept. of infectious disease, outpatient dept. of respiratory care, stomatology/endoscopic room  
|                    | Febrile outpatient department  
|                    | Isolation ward area (including isolated intensive ICU)  
|                    | Naso-sinusosal or respiratory tract lavage  
|                    | Naso-respiratory specimen examination of suspected/confirmed patients  
|                    | Imaging examination of suspected/confirmed patients  
|                    | Cleaning of surgical instruments used with suspected/confirmed patients  |
| Level III protection | • Disposable surgical cap  
|                    | • Medical protective mask (N95)  
|                    | • Work uniform  
|                    | • Disposable medical protective uniform  
|                    | • Disposable latex gloves  
|                    | • Full face respiratory protection device or powered air-purifying respirator  
|                    | When the staff performs operations such as tracheal intubation, tracheotomy, bronchoscopy, gastroenterological endoscopy, etc., during which the suspected/confirmed patients may spray or splash respiratory secretions or body fluids/liquid  
|                    | When the staff performs surgery and aspiration for confirmed/suspected patients  
|                    | When the staff carries out PPE for COVID-19  
|                    | Staff collecting respiratory specimens  

COVID-19: Personal Protection Equipment (health worker)

COVID-19: Self-evaluation

- **Indications for home care**
  
  T<38℃, mild symptom, no obvious SoB or dyspnea
  
  No travel to epidemic area, no contact people from epidemic area, no clustering onset within 14 days before illness
  
  No chronic respiratory, cardiovascular disease…
  
  Not pregnant women, children, or the elderly
  
- **Indications for seeking medical advice** (one of following criteria)
  
  T≥38℃, no symptom improvement or deterioration after 1~2 days home care
  
  Travel to epidemic area or contact people from epidemic area recently
  
  Close contact with symptomatic patients
  
  The elderly, pregnant women, children, patients w/ chronic diseases (lung, heart, liver, kidney) or immunocompromise
COVID-19: Screen Criteria in Clinical Settings

- **Epidemiological history**
  - Travel or residence in epidemic area within 14 days before illness
  - Contact with COVID-19-infected persons within 14 days before illness
  - Contract with patients presenting symptoms, who travel to epidemic area within 14 days before illness
  - **Clustering onset** ($\geq 2$ symptomatic cases within 2 weeks in small area)

- **Clinical manifestation**
  - Fever and/or respiratory symptoms
  - Imaging features of COVID-19 pneumonia
  - Total leukocytes $-\downarrow$, lymphocyte $-\downarrow$ (early stage)

- **Confirmed Case**
  - Real-time RT-PCR for COVID-19 nucleic acid: positive
  - Gene sequencing: highly homologous with COVID-19
  - COVID-19 specific IgM and IgG: positive

- **Suspected Case**
  - 1 epidemiological criterion + 2 clinical criteria
  - OR 3 clinical criteria
COVID-19: Fever Clinic

Screening Process for COVID-19

- Patient w/ fever
- Exclusion (Normal clinic)
- Suspected
- Confirmed
- Positive
- Negative
- Designated hospitals
- Medical Observation
  - Rule out criteria: nucleic acid test (-) ≥ 2 (≥ 24h interval)
  - IgM and IgG (-) after 7 days from onset

Isolation & Report to CDC

- Specimens collection
- Nucleic acid test

Fever Clinic Layout

- Three zones, Two passages

COVID-19: Fangcang Shelter hospital

Figure 2: Key characteristics and essential functions of Fangcang shelter hospitals

- Caring 12,000 COVID-19 pts

COVID-19: Fangcang Shelter hospital

<table>
<thead>
<tr>
<th>Admission Criteria</th>
<th>Reason for criterion</th>
<th>Alternative care pathway if criterion is not met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive COVID-19 test with mild signs or symptoms (mild clinical symptoms, imaging shows no signs of pneumonia) or moderate signs or symptoms (fever, respiratory tract symptoms, imaging shows pneumonia)</td>
<td>The primary purpose of the Fangcang shelter hospitals is to greatly expand capacity to care for COVID-19 patients with mild to moderate signs or symptoms</td>
<td>Patients with severe signs or symptoms are referred to higher-level hospitals; suspected cases are referred to quarantine locations with continued community screening for COVID-19</td>
</tr>
<tr>
<td>Ability to walk and live independently</td>
<td>Fangcang shelter hospitals cannot provide intensive care for patients who cannot take care of themselves</td>
<td>Referred to higher-level hospitals</td>
</tr>
<tr>
<td>Absence of severe chronic disease, including hypertension, diabetes, coronary heart disease, malignancy, structural lung disease, poliomyelitis, heart disease, and immunosuppression</td>
<td>Early evidence suggests that patients with underlying health conditions, such as hypertension, diabetes, and cardiovascular disease, are more likely than patients without these comorbidities to develop severe COVID-19</td>
<td>Referred to higher-level hospitals</td>
</tr>
<tr>
<td>No history of mental health conditions</td>
<td>Fangcang shelter hospitals do not have the capacity to treat psychiatric diseases; in addition, early evidence suggests that patients with some mental health conditions, such as anxiety disorders, are more likely to develop severe COVID-19</td>
<td>Referred to higher-level hospitals</td>
</tr>
<tr>
<td>&lt;65 years old</td>
<td>Elderly evidence suggests that older patients are at considerably increased risk of developing severe COVID-19</td>
<td>Referred to higher-level hospitals</td>
</tr>
<tr>
<td>Negative influenza test</td>
<td>Admission to Fangcang shelter hospitals should not increase the risk of influenza co-infection</td>
<td>Referred to higher-level hospitals</td>
</tr>
<tr>
<td>SpO2 &gt;93% and breathing rate &lt;30 breaths per minute in resting state</td>
<td>Oxygen saturation and breathing rate are important physiological parameters of the respiratory and circulatory system, and are used to gauge the severity of COVID-19; early evidence suggests that patients with dyspnea and hypoxia (SpO2 &lt;93%) should receive supplemental oxygen and be admitted to an isolation ward</td>
<td>Referred to higher-level hospitals</td>
</tr>
</tbody>
</table>

These criteria were applied during the COVID-19 outbreak in Wuhan, China from February to March, 2020. COVID-19-coronavirus disease 2019, SpO2=Arterial oxygen saturation.

Table: Fangcang shelter hospital admission criteria


Outline

- What is the coronavirus disease 2019 (COVID-19)?
- How to prevent & identify COVID-19 infection?
- How to control COVID-19 pandemic?
- How to manage patients with COVID-19?
- COVID-19 & Cardiovascular Disease
Wuhan, China (武汉 [武汉]，中国)

Largest city in Hubei, most popular in Central China
Population: > 11 million
"the Chicago of China" (location & transportation)
GDP of US$22.4 billion in 2018

From Wikipedia-Wuhan

China’s Efforts on COVID-19 Pandemic

Dec 26
4 unusual cases of pneumonia (3 in the same family) reported to local CDC by JX Zhang, MD

Jan 3
Initiated emergency monitoring, case investigation, close contact management & market investigation

Jan 12
2019-nCoV sequences firstly shared to WHO

Jan 16
2019-nCoV RT-PCR assays distributed to Hubei

Jan 23
Wuhan city locked down

Apr 8
Wuhan's lockdown easing

Jan 10: WHO global alert
WHO declares a "public health emergency of international concern"

Jan 23: Wuhan lockdown
First 1000-bed hosp. start to build

Feb 3
First 3 temporary hosp. start to build

Feb 7
Medical teams from other 19 provinces and regions arrived in Hubei Province

China's Efforts on COVID-19 Pandemic

Action Against COVID-19: Lock Down & Shut Down

The Black Death Quarantine


Potential infected 96%

Travel ban & national emergency response delayed
the growth and limited the size of the COVID-19 epidemic

Action Against COVID-19: Intensive Testing

- **Rapid (15 min) SARS-CoV-2 IgM-IgG combined antibody test kit**
  - Sensitivity 89%
  - Specificity 91%
  - 20s per scan, accuracy 96%

- **Real-Time Fluorescent RT-PCR Kit for Detecting SARS-CoV-2**
  - FDA approval (EUA): Mar-27

- **Artificial intelligence assisted COVID-19 imaging diagnosis**
  - 20s per scan, accuracy 96%

Action Against COVID-19: Medical Backup & Free for Treatment

- 330 medical teams, 416,000 medics
- 40,000 hospitals beds
- 70,000 quarantine beds
- Daily mask production 8 to 55.4 million within 1 month

Medical team from Beijing Anzhen Hospital
11 health workers, 85 days in Wuhan

Liang Tang, MD
MHI scholar (17~19)
Xiangya Hospital 52 days in Wuhan
Action Against COVID-19: International Support

From 71 counties & 9 international organizations

WHO-China Joint Mission

Dr. Lipkin & Dr. Zhong sharing opinions on COVID-19

Overseas Chinese people & students donate PPE to the frontline in Wuhan

COVID-19: Second Wave in China?

• Containment measures easing gradually with ultra-caution in China

  Close monitoring, extensive testing & contract tracing to new cases
  Maintaining social-distancing practices (some factories reopened, schools closed)
  Closing borders (returning residents quarantined for 14 days)

  Vaccines undergoing research and development

Health Code

Red: confirmed cases (To Yellow: discharge+14 days quarantine; To Green: another 14 days quarantine at home)
Yellow: suspected cases or turning from Red (To Green: RT-PCR negative+14 days quarantine)
Green: remain in safe area, turning from Red/Yellow--return to work, use public transportations & cross provincial borders

Staff at a car-manufacturing plant in Wuhan, social-distancing measures during lunch break

https://www.nature.com/articles/d41586-020-00938-0
Outline

• What is the COVID-19?
• How to prevent & identify COVID-19 infection?
• How to control COVID-19 pandemic?
• How to manage patients with COVID-19?
• COVID-19 & Cardiovascular Disease

COVID-19: General Treatment

• Rest in bed with supportive treatment
  Sufficient energy supply, water and electrolyte balance
• Monitor
  Vital signs, O₂%
  Blood/urine routine, CRP, biochemical indicators, coagulation, ABG, chest imaging, cytokine
• O₂ therapy
  Nasal cannula, mask O₂, high-flow nasal cannula O₂ therapy
COVID-19: Antiviral Therapy

<table>
<thead>
<tr>
<th>Medication</th>
<th>Dosage and usage (for adult)</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-interferon</td>
<td>5 million U + 2ml sterile water, 2 times/day, inhalation (in negative pressureward)</td>
</tr>
<tr>
<td>Lopinavir/Ritonavir</td>
<td>200 mg/50 mg/capsule, 2 capsules each time, 2 times/day, treatment courses 10 days</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>500 mg each time, 2~3 times/day, intravenous infusions, treatment courses ≤ 10 days, Recommend Ribavirin combination with Interferon or Lopinavir/Ritonavir</td>
</tr>
</tbody>
</table>
| Chloroquine phosphate       | Weight>50kg: 500 mg each time, 2 times/day for 7 days  
Weight<50kg: 500 mg each time, 2 times/day for day 1 and day 2; 1 time/day for day 3~7  
Contraindication: heart disease |
| Abidol                      | 200 mg each time, 3 times/day, treatment courses 10 days                                      |

**Attention:**

Adverse reactions, contraindications, interactions with other drugs, fetal toxicity
No recommendation for ≥ 3 antivirus drugs at the same time
Avoid inappropriate use of antibacterial drugs

### COVID-19: Developing Vaccines

<table>
<thead>
<tr>
<th>Vaccine Platforms, Their Attributes, and the Status of Tested Candidates†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Technology</strong></td>
</tr>
<tr>
<td>DNA</td>
</tr>
<tr>
<td>mRNA</td>
</tr>
<tr>
<td>Nucleic acid</td>
</tr>
<tr>
<td>Inactivated virus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Low-dose Group (N=36)</th>
<th>Middle-dose Group (N=36)</th>
<th>High-dose Group (N=36)</th>
</tr>
</thead>
</table>

A single-center, open and dose-escalation phase I clinical trial for recombinant novel coronavirus vaccine (adenoviral vector) in healthy adults aged between 18 and 60 years

Antidote: 28 days post injection
SAE 6 months post injection
Neutralizing antibody against SARS-CoV-2
Adverse reactions 7 days post injection
Specific T cell response 28 days and month 6 post injection
Changes of the laboratory safety examinations

By April 2, all eligible volunteers got vaccine injection
18 volunteers finished isolation with good conditions

Nicole, et al. NEJM, March 30, 2020

† Attributes refer to general attributes of the platform, and assessments are not intended as comments about a particular candidate. NAIO: National Institute of Allergy and Infectious Diseases, and NIH: National Institutes of Health.
COVID-19: Traditional Chinese Medicine Treatment

- **Utilization** (w/ or w/o western medicine) > 90% in confirmed cases
- **Mild type/recovery phase**: w/ or w/o western medicine → relief symptom, reduce progression to severe type
- **Severe type**: Inhibition of cytokine storm

**Three Drugs, Three Prescriptions**

1. 芦荟清瘟汤: 生黄、麦冬、金银花、连翘、厚朴、甘草、大黄、玄参、荆芥、金银花、连翘等组成。
2. 化瘟败毒汤: 生黄、麦冬、金银花、连翘、厚朴、甘草、大黄、玄参、荆芥、金银花、连翘等组成。
3. 宣肺败毒汤: 生黄、麦冬、金银花、连翘、厚朴、甘草、大黄、玄参、荆芥、金银花、连翘等组成。

COVID-19: Treatment of Severe & Critically Severe Cases

- **Principles**
  - Treatment: symptom, underlying diseases
  - Prevention: complications, secondary infections
  - Support: multiple organ function

- **Management**  
  - Multidisciplinary Collaboration & Management

  | Respiratory support | Recovered patients’ plasma therapy |
  | Circulatory support | Blood purification treatment |
  | Renal failure and renal replacement therapy | Immunotherapy |
Severe & Critically Severe COVID-19: Respiratory Support

- **Standard oxygen therapy**
  - Nasal cannula, mask O₂
  - Persistent dyspnea, hypoxemia

- **Advanced oxygen therapy**
  - High-flow nasal cannula O₂, non-invasive mechanical ventilation
  - No improvement or worsen within 1-2 hrs

- **Invasive mechanical ventilation**
  - Lung protective ventilation: small tidal volume, low plateau pressure
  - Lung expansion: severe adult respiratory distress syndrome (ARDS)
  - Prone position ventilation: >12 hrs/d
  - ECMO: prone ventilation is not effective

- **Salvage treatment**
  - High-flow nasal cannula O₂
  - Persistent dyspnea, hypoxemia
  - Keep airway warm, humid, avoid prolonged sedation, early pulmonary rehabilitation
  - Keep airway warm, humid, avoid prolonged sedation, early pulmonary rehabilitation
  - Closed sputum suction, bronchoscopy if necessary
  - Lung expansion: severe adult respiratory distress syndrome (ARDS)
  - Prone position ventilation: >12 hrs/d
  - ECMO: prone ventilation is not effective
  - Indications: FiO₂ > 90%, oxygenation index < 80 mmHg, lasting > 3~4 hrs;
  - Mode: VV mode: simple respiratory failure, plateau pressure ≥ 35 cm H₂O;
  - VA mode: circulatory support needed
  - Weaning trails: underlying disease controlled, cardiopulmonary function began to recover

Positive pressure ventilation might induce viral aerosol formation!

---

Severe & Critically Severe COVID-19: Circulatory Support

- **Consider to use**
  - Adequate fluid resuscitation, microcirculation improvement and vasoactive agents

- **Close monitor**
  - BP, HR, urine output, ABG (lactic acid, base excess)

- **Fluid balance**
  - Noninvasive/invasive hemodynamic monitoring (Doppler echo, echo, invasive BP, PiCCO)

- **Attention**: septic shock, GI bleeding, severe heart failure

PiCCO, pulse-induced continuous cardiac output
Severe & Critically Severe COVID-19: Renal Failure Treatment

- **Etiological treatment** (e.g., hypoperfusion, drugs)
- **Monitoring**
  
  Fluid balance, acid-base balance and electrolyte balance
  
  Nitrogen balance, calorie and minerals supplement
- **Renal replacement therapy (CRRT)**
  
  **Indications:**
  ① hyperkalemia; ② acidosis; ③ pulmonary edema or excessive water load;
  ④ fluid management when multiple organ dysfunction occurs

Severe & Critically Severe COVID-19: Recovered Patients’ Plasma Therapy

- **Indication:** severe or critically severe patients with rapid disease progression
- **Contraindication**
  
  - Allergy history of plasma, sodium citrate and methylene blue
  - Autoimmune system diseases or selective IgA deficiency
- **Infusion dosage:** ≥ 400 ml/fusion, or ≥ 200 ml/fusion * multiple times
- **Donor**
  
  Age 18~55 y/o, weight > 50kg (male)/45kg (female)
  
  ≥ 3 weeks from onset of symptoms
  
  Meeting discharge criteria
  
  No history of blood transmitted diseases
  
  Lab test for SARS-CoV-2 negative
  
  Nucleic acid test, 160-/320-fold dilution for qualitative test of virus-specific IgG & IgM, viral neutralization test
Severe & Critically Severe COVID-19: Blood Purification Treatment

- **Component**
  Plasma exchange, absorption, perfusion, blood/plasma filtration…

- **Objective**
  Remove inflammatory factors, reduce the “Cytokine Storm”

- **Indication**
  Early and mid-term cytokine storm

Severe & Critically Severe COVID-19: Immunotherapy

- **Indication**
  Extensive lung lesion, elevated Interleukin-6 levels

- **Tocilizumab**
  First dose 4-8 mg/kg, recommended dose 400 mg + 0.9% saline to 100 ml, infusion time > 1 hr
  
  If first medication ineffective, try second time after 12 hrs (same dose)
  
  Cumulative administrations ≤ 2 times, max. single dose ≤ 800 mg
  
  Attention to allergic reactions, not recommended for active infections
Severe & Critically Severe COVID-19: Other Treatments

- **Glucocorticoids**  
  **Indication:** progressive deterioration (oxygenation, imaging, inflammatory response)  
  Short-term (3~5 days) use, Dosage: methylprednisolone ≤ 1~2 mg/kg/day  
  **Large doses is not recommended:** delay removal of coronavirus

- **Intestinal micro-ecological regulator**  
  Maintain intestinal micro-ecological balance, prevent secondary bacterial infections

- **Intravenous gamma globulin**

- **Pregnant women:** pregnancy termination or cesarean delivery (preferred)

- **Psychological counseling:** anxiety, fear

---

COVID-19: Discharge Criteria & Precautions

- **Discharge Criteria** (meet all of below conditions)
  - Body temperature: normal for > 3 days
  - Respiratory symptoms: significant improvement
  - Pulmonary imaging: marked improvement
  - Nucleic acid test: negative for two consecutive times (> 24 hrs interval)

- **Precautions after discharge**
  - Share medical records to basic medical and health institutions
  - **Recommend isolation** and health monitoring for 14 days
  - Follow up in the 2nd and 4th week after discharge
Outline

• What is the coronavirus disease 2019 (COVID-19)?
• How to prevent & identify COVID-19 infection?
• How to control COVID-19 pandemic?
• How to manage patients with COVID-19?
• COVID-19 & Cardiovascular Disease

COVID-19 & Cardiovascular Disease

• Common comorbidities
  
  HTN (14~22%), DM (6~11%), CVD (4~7%), respiratory disease (1~3%)


• Acute cardiac injury
  
  Common in severe cases, even in patients without pre-existing CVD

  Presenting cardiac symptoms & seeing a cardiologist, then diagnosis

• Patients with pre-existing CVD
  
  More likely to be infected, developed severe symptoms, even had high mortality

• Patients taking antiviral drugs
  
  Drug-related heart damage should not be ignored

COVID-19 & Myocardial Injury: Potential Mechanism

- Virus invades myocardium, leading to myocardial injuries and myocarditis
- Cytokine storm
  - Pro-inflammatory factors ↑↑ (dose-effect)
  - Anti-inflammatory factors ↑ (feedback & adjustment)
- Pulmonary infectious
  - Hypoxemia/hypotension, imbalance of myocardial O2 supply


Withdrawal of ACEi or ARB in COVID-19 patients? No, robust evidence is lacking!

Clerkin et al. European Heart Journal (2020) 0, 1–3
COVID-19: Critical Cardiovascular Disease Management

Chinese Society of Cardiology Expert Consensus on Managing CVD during COVID-19 Epidemic

Table 1. Patients with severe emergent cardiovascular diseases for whom hospitalization and conservative medical treatment is recommended during COVID-19 epidemic.

<table>
<thead>
<tr>
<th>Patients with severe emergent cardiovascular diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patients with STEMI for whom thrombolytic therapy is indicated</td>
</tr>
<tr>
<td>2. STEMI patients presenting either exceeding the optimal window of time for revascularization but yet with worsen symptoms, such as severe chest pain, continuous ST-segment elevation, or myocardial infection-related mechanical complications</td>
</tr>
<tr>
<td>3. High risk NSTE-ACS patients (GRACE score ≥ 140)</td>
</tr>
<tr>
<td>4. Patients with uncomplicated or unstable Type B acute dissecting</td>
</tr>
<tr>
<td>5. Patients with acute pulmonary embolism</td>
</tr>
<tr>
<td>6. Patients with acute exacerbation of heart failure</td>
</tr>
<tr>
<td>7. Patients with hyperacute myocardial infarction</td>
</tr>
<tr>
<td>STEMI, ST-segment elevation myocardial infarction; NSTE-ACS, non-ST elevation acute coronary syndrome; GRACE, Global Registry of Acute Coronary Events</td>
</tr>
</tbody>
</table>

Table 2. Severe cardiovascular diseases requiring urgent or emergent intervention or surgery.

<table>
<thead>
<tr>
<th>Patients with severe cardiovascular diseases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Acute STEMI with hemodynamic instability</td>
</tr>
<tr>
<td>2. Left-threatening NSTE-ACS indicated for urgent revascularization</td>
</tr>
<tr>
<td>3. Unstable Type A or complex Type B acute aortic dissection</td>
</tr>
<tr>
<td>4. Hypeacute myocardial infarction complicated with severe or unstable hemodynamics; modulated implantation of a temporary pacemaker (implantation as it is feasible), or, if indicated, permanent pacemaker</td>
</tr>
<tr>
<td>5. Pulmonary embolism presenting with hemodynamic instability for whom regular intravenous thrombolytic therapy might lead to excessive risk of intimal bleeding, and trans-catheter low-dose thrombolytic in the pulmonary artery may be required</td>
</tr>
<tr>
<td>6. STEMI, ST-segment elevation myocardial infarction; NSTE-ACS, non-ST elevation acute coronary syndrome</td>
</tr>
</tbody>
</table>

COVID-19: Unanswered Questions

Panel 1. Key unanswered questions of the Covid-19 outbreak

- **Epidemiology**
  - What is the optimal strategy for identifying contacts of infected individuals?
  - To which extent has the virus mutated during the global transmission?
  - What is the proportion of super-spreaders among the whole cohort of patients with Covid-19?
- **Virology and Clinical courses**
  - Is there evidence of pre-symptomatic viral shedding?
  - What is the time point of viral shedding and what is the association with disease progression?
  - Are patients with a relapse of positive viral RNA findings contagious when discharged home?
  - What is the natural course of severe and non-severe cases?
  - What is the characteristic and mechanism of mucus hypersecretion in small airways?
  - How does SARS-CoV-2 result in lymphopenia and inflammatory cytokine storm?
  - What is the most valuable biomarker for predicting the clinical outcomes of Covid-19?
  - Could artificial intelligence aid in the diagnosis and phenotyping Covid-19?
- **Treatment**
  - Will inhibitors of viral replication be effective in the clearance of Covid-19?
  - What are the most cost-effective management of Covid-19?
  - When should be the optimal timing and duration for intubation?
  - Which medication(s) may be useful to suppress the inflammatory cytokine storm?

Wei-jie Guan et al. European Respiratory Journal 2020
COVID-19: Free Online Resources

- Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (7th edition)
  published by China National Health Commission on March 4, 2020

- Guidance for Corona Virus Disease 2019: Prevention, Control, Diagnosis and Management
  published by China National Health Commission
  [https://mp.weixin.qq.com/s/bwlkBTJLe2oORWRUs1N5yQ](https://mp.weixin.qq.com/s/bwlkBTJLe2oORWRUs1N5yQ)

  published by WHO-China Joint Mission

- Handbook of COVID-19 Prevention and Treatment
  published by Jack Ma Foundation, Alibaba Foundation, The First Affiliated Hospital, Zhejiang University School of Medicine

Questions & Answers

Thanks for your attention