Diagnosis and treatment Protocol of COVID-19

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Epidemiological characteristics

(1) The source of infection.

- The COVID-19 patients;
- Asymptomatic infected people can also be a source of infection.

(2) Route of transmission

- Respiratory droplets and close contact are the main routes of transmission.
- There is the possibility of aerosol transmission in a relatively closed environment for a long-time exposure to high concentrations of aerosol.
- As the novel coronavirus can be isolated in feces and urine, attention should be paid to feces or urine contaminated environment that leads to aerosol or contact transmission.

(3) susceptible population.

- All the population are generally susceptible.

Pathological changes

Pathological findings from limited autopsies and biopsies gave the evidence that COVID-19 mainly causes lung damage.

1. Lungs

- The varying degrees of lungs solid changes.
- Alveolar damage involves fibro myxoid exudation and hyaline membrane formation.
- The exudates are composed of monocytes and macrophages.
- Alveolar interstitium is marked with vascular congestion and edema, infiltration of monocytes and lymphocytes, and vascular hyaline thrombi.
- The lungs are laden with hemorrhagic and necrotic foci, hemorrhagic infarction.
- The bronchi are filled with mucus and mucus plugs.
- On electron microscopy, cytoplasmic virions are observed in the bronchial epithelium and type II alveolar epithelium.

Pathological changes

2. Spleen, Hilar lymph nodes and bone marrow

- The spleen is evidently shrunk with Lymphocytopenia and focal hemorrhage and necrosis, and macrophage proliferation and phagocytosis.
- Lymph nodes are found with sparse lymphocytes and occasional necrosis.
- CD4+ and CD8+ T cells are present in reduced quantity in the spleen and lymph nodes.
- Pancytopenia is identified in bone marrow.

Clinical manifestations

- The incubation period: the incubation period is 1-14 days, mostly 3-7 days.
- Clinical Features:
  - Fever, dry cough, fatigue as the main performance.
  - In severe cases, dyspnea or hypoxemia usually occur one week after the onset of the disease.
- The severe or critical case may have low fever, or even no fever.
- The elderly patients and those with chronic underlying diseases have poor prognosis.

Laboratory test

- In most patients, white blood cells was normal or decreased, with the lymphocyte count decreased.
- C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were elevated.
- Some patients show an increase in liver enzymes, lactate dehydrogenase (LDH), muscle enzymes and myoglobin.
- In severe cases, D-dimer increased progressively.
- Elevated troponin is seen in some critically ill patients.
- Severe and critical patients often have elevated inflammatory factors.

Virological and serological findings

- Virological detection:
  - Viral RNA can be detected in nasopharyngeal swabs, sputum, lower respiratory tract secretions, blood, feces and other specimens using RT-PCR or NGS.
  - Recommend to collect lower respiratory tract samples (sputum or air tract extraction) to increase the sensitivity.

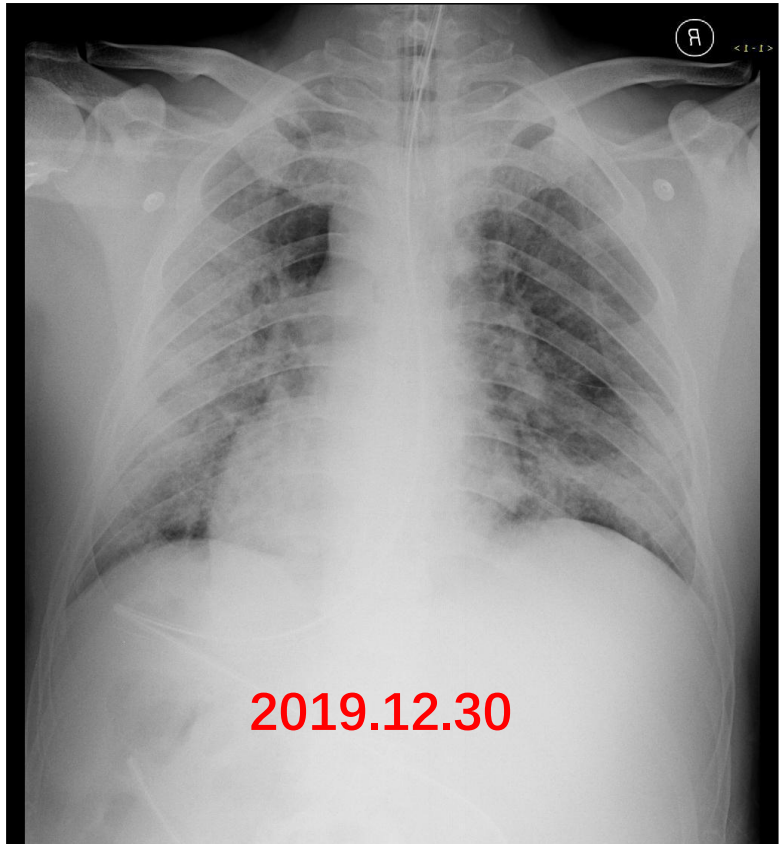
- Serological test:
  - Viral specific IgM antibody becomes detectable around 3-5 days after onset;
  - Viral specific IgG antibody reaches a titration of at least 4-fold increase during convalescence compared with the acute phase.

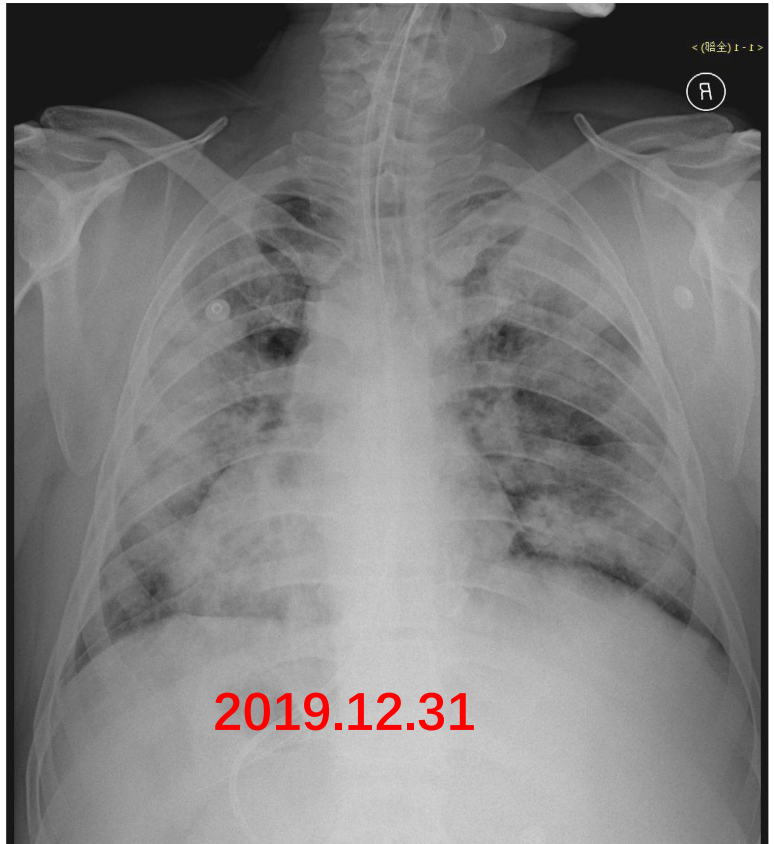
Chest imaging

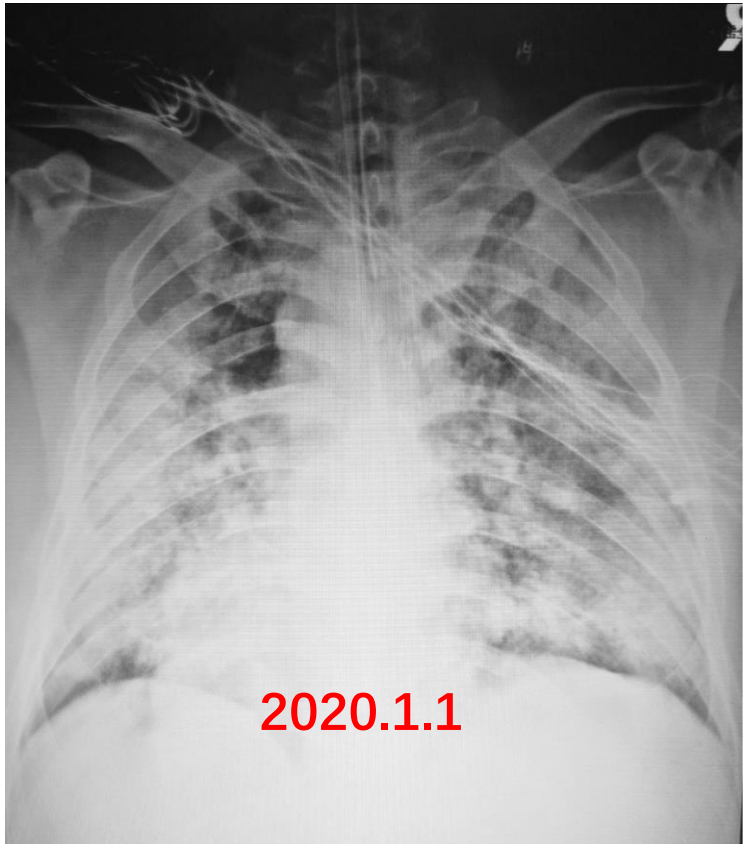
- In the early stage, there were multiple spotted shadows and interstitial changes, which were obvious in the extraneous lung.
- Further, multiple ground-glass shadows and infiltration shadows were found in both lungs.
- Lung consolidation was found in severe cases.

X-ray

- Male, 44 years old, fever, fatigue, treatment progress
- infiltration shadows appear in the lungs, often initially close to the pleura, and gradually develop toward the center







Progressive CT findings

8 dyas after onset
subpleural distribution ground-glass shadows

20 dyas after onset
The infiltration lesion develops to the center and presents a consolidation

Diagnostic criteria

1. suspected cases:

- Epidemiological history
  - ① History of travel to or residence in communities where cases reported within 14 days prior to the onset of the disease;
  - ② In contact with viral RNA positive people within 14 days prior to disease onset;
  - ③ In contact with patients who have fever or respiratory symptoms from communities confirmed cases reported within 14 days before disease onset;
  - ④ Clustered cases (2 or more cases with fever and/or respiratory symptoms in a small area such as families, offices, school room etc. within 2 weeks).

Diagnostic criteria

1. suspected cases.

- Clinical features
  - ① fever and/or respiratory symptoms;
  - ② imaging characteristics;
  - ③ The white blood cells was normal or decreased, with lymphocyte decreased.

Diagnostic criteria for suspected cases:

- Any one of the epidemiological history with any two of the clinical features.
- All three clinical features.

Diagnostic criteria

2. Confirmed cases:

- Suspected cases with one of the following virological or serological evidences:
  - Real-time fluorescent RT-PCR indicates positive for novel coronavirus RNA;
  - Viral gene sequence is highly homologous to known novel coronaviruses;
  - Viral specific IgM and IgG are detectable in serum;
  - Viral specific IgG is detectable from negative to positive, or
  - Viral specific IgG antibody reaches a titration of at least 4-fold higher in the recovery stage than in the acute stage.

Clinical Types

(1) Mild:

The clinical symptoms were mild, and there was no sign of pneumonia on imaging.

(2) Moderate:

Showing fever and respiratory symptoms with radiological findings of pneumonia.

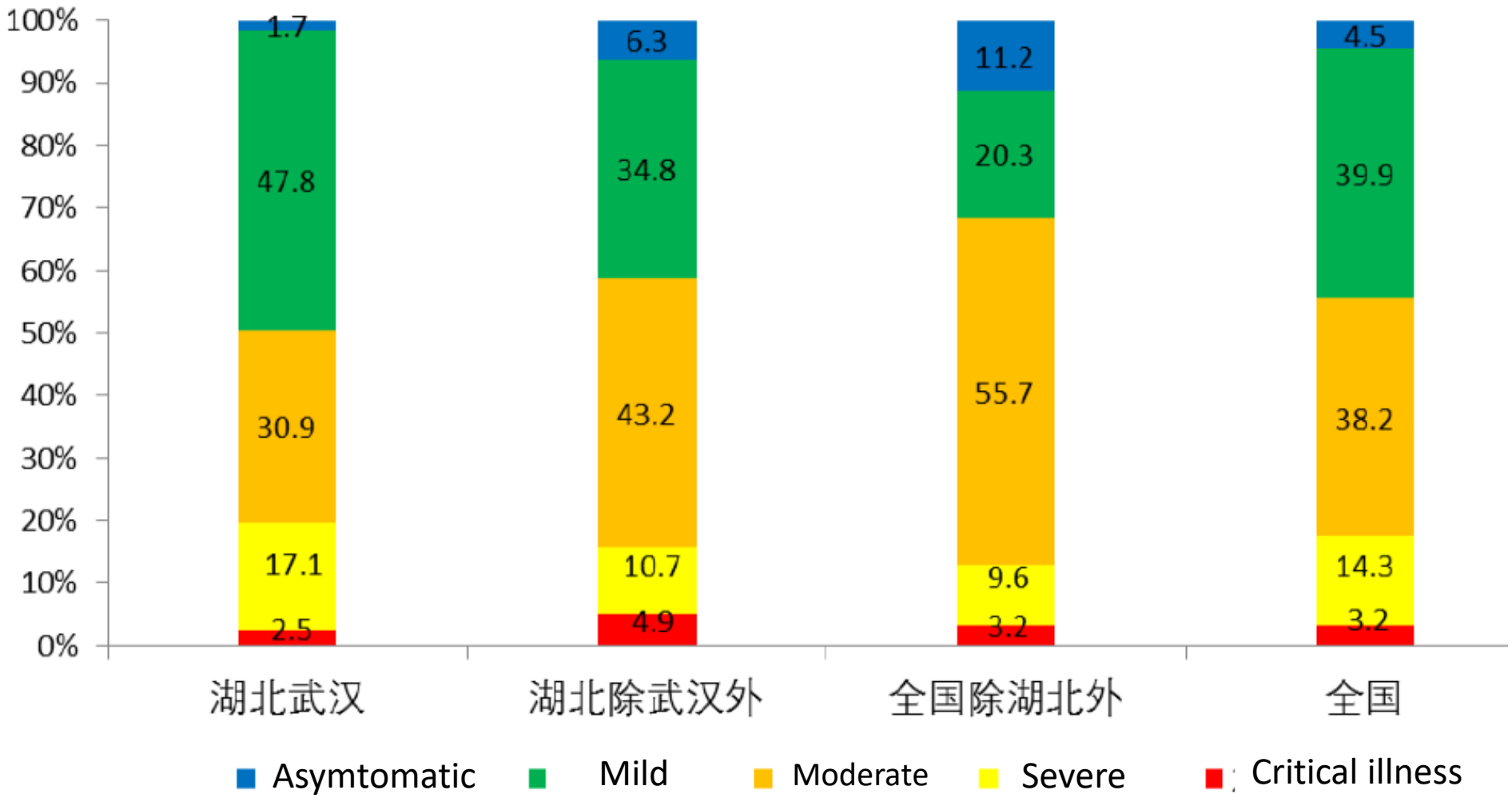
(3) Severe. In accordance with any of the following:

1. Shortness of breath (RR ≧ 30 breaths/min);
2. In resting state, oxygen saturation ≤ 93%;
3· Arterial partial pressure of oxygen (PaO_2)/ fraction of inspired oxygen (FiO_2) ≦ 300mmHg (l mmHg=0.133kPa).
4. Cases with chest imaging showed obvious lesion progression more than 50% within 24-48 hours.

(4) Critical: One of the following:

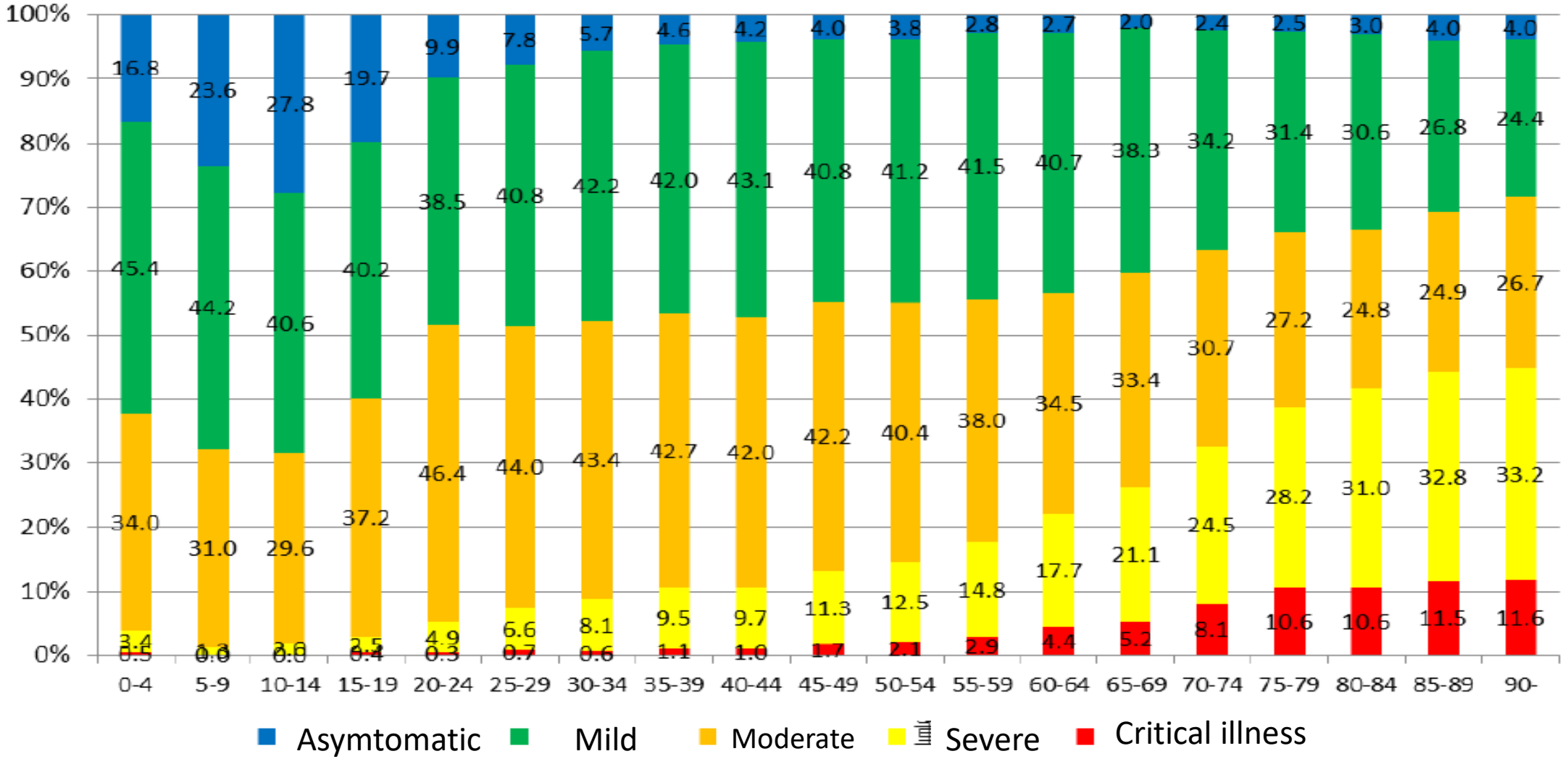
1. Respiratory failure, requiring mechanical ventilation;
2. Shock;
3. With other organ failure that requires ICU care.

The proportion of clinical types in different regions



China CDC/NHC 20200303

The proportion of severe diseases increases with age



China CDC/NHC 20200303

The proportion of deaths in different age groups

China CDC/NHC 20200303

Early warning indicators of severe and critical cases

- The peripheral blood lymphocytes decrease progressively;
- Progressively elevation of inflammatory factors, such as IL-6 and C-reactive proteins;
- Lactate sustained or progressive elevation;
- Lung lesions develop rapidly in a short period of time.

General management

- Rest and symptomatic support therapy; sufficient caloric; water and electrolyte;
- Closely monitoring vital signs and oxygen saturation.
- Monitoring lab test: blood routine result, urine routine result, c-reactive protein (CRP), biochemical indicators (liver enzyme, myocardial enzyme, renal function etc.), coagulation function, arterial blood gas analysis, chest imaging and cytokines detection if necessary.
- Early oxygen therapy and airway drainage.

General management

- Antiviral therapy:

  Some drugs that are already on market can be tried to treat COVID-19 and the efficacy of the drugs need to be evaluated in clinical application.

  - Alpha-interferon: 5 MU, atomization inhalation twice daily;
  - Kaletra (Lopinavir/ritonavir)
  - Chloroquine phosphate
  - Arbidol:

- Antibiotic drug treatment: Rational use of antimicrobial agents.

Treatment of severe and critical cases

- Treatment principle: On the basis of symptomatic treatment, the prevention of complications, treatment of underlying diseases, prevention of secondary infections, and timely organ function support should be reinforced.
  1. Respiratory support:
  2. Circulatory support:
  3. Renal failure and renal replacement therapy:
  4. Convalescent plasma treatment:
  5. Blood purification treatment:
  6. Immunotherapy:
  7. Other therapeutic measures

Respiratory support: Oxygen therapy

- Nasal cannulas or masks for oxygen inhalation:
- High-flow nasal-catheter oxygenation or noninvasive mechanical ventilation:
  - When respiratory distress and/or hypoxemia cannot be alleviated by oxygen therapy.
- Invasive mechanical ventilation:
  - If conditions do not improve or even get worse within 1-2 hours.
  - Use closed sputum suction according to the airway secretion, if necessary, administer appropriate treatment based on bronchoscopy findings.
- Rescue therapy:
  - Pulmonary reconstruction is recommended for patients with severe ARDS.
  - With sufficient human resources, prone position ventilation should be performed for more than 12 hours per day.
  - If prone position ventilation did not work, extracorporeal membrane oxygenation (ECMO) should be considered as soon as possible.

Convalescent plasma treatment:

- Indications
  - Patients with rapid disease progression, severe and critical illness.
  - The course of illness should not exceed three weeks;
  - The nucleic acid test was positive or other evidence of presence of viruses;

- Infusion dose
  - The usual infusion dose is 200-500 ml (4-5 ml/kg), two times

Blood purification treatment:

- It can be used for the treatment of severe and critical cases in the early and middle stages of cytokine storm.
- Including plasma exchange, absorption, perfusion and blood/plasma filtration;
- To remove inflammatory factors and block "cytokine storm“.

Other therapeutic measures:

- Glucosteroid:
  - For patients with progressive deterioration of oxygenation indicators, rapid progress in imaging and excessive activation of the body's inflammatory response
  - In a short period of time (3 to 5 days).
  - It is recommended using methylprednisolone 1-2 mg/kg/day.
  - Note that a larger dose of glucocorticoid will delay the removal of coronavirus due to immunosuppressive effects.

- Intestinal microecological regulators:
  - To maintain intestinal microecological balance and prevent secondary bacterial infections.

Traditional Chinese Medicine treatment

1. Clinical manifestations during medical observation
   - huoxiang zhengqi capsule (pill, water, oral liquid)
   - jinhua qinggan granules, lianhua qingwen capsules (granules), shufeng jiedu capsules (granules)

2. Clinical treatment phase (confirmed cases)

Conclusion

- COVID-19 is an emerging infectious disease, that many aspects still need to be elucidated, including the pathogenesis, pathology.
- Early diagnosis and early treatment is critical.
- Effective oxygen treatment are very important.
- We will update the protocol with increased understanding of the clinical manifestations and pathology of the disease, and the accumulation of experience in diagnosis and treatment.

Thanks for your attention!

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