Shanghai 2019 Expert Coronary Disease Comprehensive Treatment Consensus

Shanghai Medical Association 3/3

【Editor's note】

On March 1, the "Chinese Journal of Infectious Diseases" network hosted by the Shanghai Medical Association pre-published the "Shanghai 2019 Coronary Virus Disease Comprehensive Treatment Expert Consensus" (http://rs.yiigle.com/m/yufabiao/1183266 .htm), which has aroused widespread concern in the industry, and Shanghai TV also carried a news report last night. This consensus was composed of 30 experts representing the strongest medical force in the treatment of Shanghai's new coronavirus pneumonia, through a summary of more than 300 patients in clinical research, and fully drawing on the experience of the treatment of domestic and foreign counterparts, and finally formed the "Shanghai Plan". At the end of the article, a list of these 30 experts (18 authors and 12 consultants) from various medical institutions in Shanghai is attached.

Corona virus disease 2019 (COVID-19) was first reported in Wuhan, Hubei Province on December 31, 2019. As a respiratory infectious disease, COVID-19 has been included in the category B infectious diseases as stipulated in the Law of the People ' s Republic of China on the Prevention and Control of Infectious Diseases, and is managed as a category A infectious disease.

With the deepening of the understanding of the disease, all parts of the country have accumulated certain experience in the prevention and control of COVID-19. The Shanghai New Coronary Virus Disease Clinical Treatment Expert Group follows the national new coronavirus pneumonia diagnosis and treatment plan, and fully draws on the treatment experience of domestic and foreign counterparts to improve the success rate of clinical treatment and reduce the mortality of patients. The goal is to prevent the progress of the disease and gradually reduce the disease. The proportion of patients who are heavy, improve their clinical prognosis. On the basis of continuous optimization and refinement of the treatment plan, an expert consensus has been formed on the relevant clinical diagnosis and treatment.

1. Etiology and epidemiology

2019 novel coronavirus (2019 novel coronavirus, 2019-nCoV) is a novel coronavirus belonging to the genus β. On February 11, 2020, the International Committee on Taxonomy of Viruses (ICTV) named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Both COVID-19 patients and those with asymptomatic infections can transmit 2019-nCoV. Transmission through the respiratory tract droplets is the main route of transmission, and can also be transmitted through contact. In confined enclosed spaces, there is also the risk of aerosol transmission. 2019-nCoV can be detected in the stool, urine and blood of COVID-19 patients; some patients may still have a positive stool pathogenic nucleic acid test after the pathogenic nucleic acid test of respiratory specimens is negative. The crowd is generally susceptible. Children and infants also have the disease, but the condition is mild.

2. Clinical features and diagnosis

(1) Clinical features

The incubation period is 1-14 days, mostly 3-7 days, with an average of 6.4 days. The main manifestations are fever, fatigue, and dry cough. May be accompanied by symptoms such as runny nose, sore throat, chest tightness, vomiting, and diarrhea. Some patients have mild symptoms, and a few have no symptoms or pneumonia.

The elderly and those with basic diseases such as diabetes, hypertension, coronary atherosclerotic heart disease, and extreme obesity are prone to develop severe illness after infection. Some patients have symptoms such as dyspnea 1 week after the onset of symptoms. In severe cases, they may progress to acute respiratory distress syndrome (ARDS) and multiple organ dysfunction. The time to progress to severe disease is about 8.5 days. It is worth noting that in the course of severe and critically ill patients, the disease can be moderate to low fever, or even no obvious fever. Most patients have a good prognosis, and deaths are more common in the elderly and those with chronic underlying diseases.

Early CT examination showed multiple small patches or ground glass shadows, the internal texture of which could be thickened with grid-like strips, with obvious extrapulmonary bands. After a few days, the lesions increased and the scope expanded, showing extensive lungs, multiple ground glass shadows or infiltrating lesions, some lung consolidation, bronchial inflation often occurred, and pleural effusions were rare. A few patients progressed rapidly, and the imaging changes peaked on days 7 to 10 of the course of the disease. Typical "white lung" performance is rare. After entering the recovery period, the lesions were reduced, the scope was reduced, the exudative lesions were absorbed, some of the fibrous cords appeared, and some patients could be completely absorbed.

In the early stage of the disease, the total number of white blood cells in the peripheral blood was normal or decreased, and the lymphocyte count decreased. In some patients, abnormal liver function may occur, and the levels of lactate dehydrogenase, myozyme, and myoglobin increased; troponin levels increased. Most patients have elevated CRP and ESR levels, and normal procalcitonin levels. In severe cases, the level of D-dimer is increased, other blood coagulation indicators are abnormal, the level of lactic acid is increased, the peripheral blood lymphocytes and CD4 + T lymphocytes are progressively reduced, and electrolyte disorders, acid-base imbalance, etc. See more. In the progressive stage of the disease, there may be increased levels of inflammatory cytokines (such as IL-6, IL-8, etc.).

(2) Diagnostic criteria

1. Suspected cases: Combined with the following comprehensive analysis of epidemiological history and clinical manifestations. Any one of the epidemiological history and any two of the clinical manifestations, or no clear epidemiological history but three of the clinical manifestations, are diagnosed

as suspected cases. ① Epidemiological history: travel history or residence history of Wuhan City and surrounding areas, or other communities with case reports within 14 days before the onset of illness; history of contact with 2019-nCoV infection (positive nucleic acid test) within 14 days before onset of illness ; Contacted patients with fever or respiratory symptoms from Wuhan City and surrounding areas, or from communities with case reports within 14 days before the onset of disease; clustered onset. ② Clinical manifestations: fever and (or) respiratory symptoms; with the above-mentioned imaging features of the new coronavirus pneumonia; the number of white blood cells in the early stage of the disease is normal or decreases, and the lymphocyte count decreases.

2. Confirmed cases: A person who has one of the following etiological evidences is diagnosed as a confirmed case. ① Real-time fluorescent reverse transcription PCR test positive for 2019-nCoV nucleic acid. ② Viral gene sequencing found to be highly homologous to the known 2019-nCoV. ③ In addition to nasopharyngeal swabs, sputum is collected as much as possible, and patients with tracheal intubation can collect lower respiratory tract secretions and send viral nucleic acid test positive.

(3) Differential diagnosis

It is mainly distinguished from influenza virus, parainfluenza virus, adenovirus, respiratory syncytial virus, rhinovirus, human metapneumovirus, severe acute respiratory syndrome (SARS) coronavirus and other known viral pneumonia , With Mycoplasma pneumoniae, Chlamydia pneumonia and bacterial pneumonia. In addition, it must be distinguished from non-infectious diseases such as pulmonary interstitial lesions and organizing pneumonia caused by connective tissue diseases such as vasculitis and dermatomyositis.

(4) Clinical classification

1. Mild: Mild clinical symptoms, no pneumonia manifestations on imaging examination.

2. Common type: It has fever, respiratory tract and other symptoms. Pneumonia can be seen on imaging examination.

The early warning of the seriousness of ordinary patients should be strengthened. Based on current clinical research, the elderly (age> 65 years) with underlying disease, CD4 + T lymphocyte count <250 / μL, blood IL-6 levels increased significantly, 2 to 3 days of lung imaging revealed lesions Obvious progress> 50%, lactate dehydrogenase (LDH)> 2 times the upper limit

of normal, blood lactate ≥3 mmol / L, metabolic alkalosis, etc. are early warning indicators of severe disease.

3. Heavy: meets any of the following. ① Shortness of breath, ≥30 breaths / min; ② Arterial oxygen saturation (SaO2) ≤93% in resting state; ③ Arterial partial pressure of oxygen, PaO2) / fraction of inspired oxygen (FiO2) ≤300 mmHg (1 mmHg = 0.133 kPa). At high altitudes (altitude above 1 000 m), PaO2 / FiO2 should be corrected according to the following formula: PaO2 / FiO2 × [atmospheric pressure (mmHg) / 760].

Pulmonary imaging examination showed that the lesions significantly progressed within 24 to 48 hours> 50% were managed according to the severity.

4. Critical severity: Those who meet any of the following can be judged as critical. ① Respiratory failure occurs and mechanical ventilation is required; ② Shock occurs; ③ Other organ failures require ICU monitoring and treatment.

(5) Clinical monitoring

Monitor patients' clinical manifestations, vital signs, fluid volume in and out, gastrointestinal function and mental status every day.

Dynamic monitoring of end-of-finger oxygen saturation of all patients. For severe and critically ill patients, blood gas analysis should be carried out in time according to the change of the condition; blood routine, electrolyte, CRP, procalcitonin, LDH, coagulation function indexes, blood lactic acid, etc., should be tested at least once every 2 days; liver function, kidney function , ESR, IL-6, IL-8, lymphocyte subsets, at least once every 3 days; chest imaging examination, usually every 2 days. For patients with ARDS, it is recommended to perform routine ultrasound examination of the heart and lungs beside the bed to observe the extravascular lung water and heart parameters. For extracorporeal membrane oxygenation (ECMO) patient monitoring, refer to the ECMO implementation chapter.

3. Treatment plan

(1) Antiviral treatment

You can try hydroxychloroquine sulfate or chloroquine phosphate, Abidor oral, interferon nebulized inhalation, interferon κ is preferred, or interferon α recommended by the national program can also be used. It is not recommended to use 3 or more antiviral drugs at the same time. It should be stopped in time after the viral nucleic acid turns negative. The efficacy of all antiviral drugs still needs to be evaluated by further clinical studies.

For severe and critical viral nucleic acid positive patients, the recovery period plasma can be tried. For detailed operation and management of adverse reactions, please refer to the "Clinical Treatment Program for the Recovery Period of New Coronary Pneumonia Patients Recovered" promulgated by the National Health Commission (first trial version). Infusion within 14 days of onset may have a better effect. If viral nucleic acid is continuously detected later in the course of the disease, plasma therapy can also be used in the recovery phase of the recovered person.

(2) Treatment of light and ordinary patients

Supportive treatment needs to be strengthened to ensure adequate calories; pay attention to the balance of water and electrolytes and maintain the stability of the internal environment; closely monitor the patient's vital signs and finger oxygen saturation. Give effective oxygen therapy measures in time. In principle, antibacterial drugs and glucocorticoids are not used. It is necessary to closely observe the changes in the patient's condition. If there is significant progress in the condition and there is a risk of becoming severe, it is recommended to take comprehensive measures to prevent the disease from progressing to severe. You can use low-dose short-term glucocorticoids as appropriate). It is recommended to use heparin anticoagulation and high-dose vitamin C treatment. Low molecular weight heparin 1 to 2 sticks / d continues until the patient's D-dimer level returns to normal. Once the fibrinogen degradation product (FDP) ≥10 μg / mL and / or D-dimer ≥5 μg / mL, normal heparin is used for anticoagulation. Vitamin C is 50 to 100 mg / kg per day, intravenously, and the continuous use time aims at significantly improving the oxygenation index. If the lung lesion progresses, it is recommended to use a large dose of broad-spectrum protease inhibitor ulinastatin 600 to 1 million units / d, until the lung imaging examination is improved. Once a "cytokine storm" occurs, it is recommended to use intermittent short veno-venuous hemofiltration (ISVVH).

(3) Supporting treatment of organ function in severe and critically ill patients

1. Protection and maintenance of circulatory function: implement the principle of early active controlled fluid replacement. It is recommended to evaluate the effective volume and start fluid therapy as soon as possible after admission. Severe patients can choose intravenous route or transcolonal route for fluid resuscitation according to conditions. The supplemented liquid is preferably lactated Ringer's solution. Regarding vasoactive drugs,

norepinephrine combined with dopamine is recommended to maintain vascular tone and increase cardiac output. For patients with shock, norepinephrine is the first choice. It is recommended that small doses of vasoactive drugs be started at the same time as fluid resuscitation to maintain stable circulation and avoid excessive fluid infusion. Recommend the use of drugs that protect the heart of severe and critically ill patients, and try to avoid the use of sedative drugs that have an inhibitory effect on the heart. For patients with sinus bradycardia, isoproterenol can be used. It is recommended that for patients with sinus rhythm, heart rate <50 beats / min and hemodynamic instability, intravenous pumping of low dose isoproterenol or dopamine to maintain heart rate is about 80 beats / min.

2. Reducing pulmonary interstitial inflammation: 2019-nCoV causes severe pulmonary interstitial lesions that will cause deterioration of lung function. It is recommended to use large dose of broad-spectrum protease inhibitor ulinastatin.

3. Protection of kidney function: It is recommended to use reasonable anticoagulation therapy and appropriate liquid therapy as soon as possible. Please refer to the chapter of "Prevention of Cytokine Storm" and the Protection and Maintenance of Circulatory Function.

4. Protection of intestinal function: Prebiotics can be used to improve the intestinal microecology of patients. Use raw rhubarb (15 ~ 20 g plus 150 ml of warm boiling water) or Dachengqi decoction orally or enema.

5. Nutritional support: Gastrointestinal nutrition is preferred, via nasal feeding or via jejunal route. The first choice is whole protein nutritional preparation, with an energy of 25 ~ 35 kcal / kg per day (1 kcal = 4.184 kJ).

6. Prevention of "cytokine storm": It is recommended to use high-dose vitamin C and unfractionated heparin for anticoagulation. Large-dose vitamin C is intravenously injected at 100-200 mg / kg per day. The continuous use time aims at significantly improving the oxygenation index. Dose broad-spectrum protease inhibitor ulinastatin, given 1.6 million units, once every 8 h, under mechanical ventilation, when the oxygenation index> 300 mmHg can be reduced to 1 million units / d. Anticoagulation can be taken Treatment protects endothelial cells and reduces cytokine release. When FDP ≥10 μg / mL and / or D-dimer ≥5 μg / mL, heparin (3 ~ 15 IU / kg per hour) is used for anticoagulation. Heparin is used for the first time. The patient's coagulation function and platelets must be rechecked after 4 h. ISVVH is used, 6 to 10 h per day.

7. Sedative muscle relaxation and artificial hibernation therapy: patients with mechanical ventilation or receiving ECMO should be sedated on the basis of analgesia. For patients with severe man-machine confrontation when establishing artificial airways, it is recommended to use small doses of muscle relaxants in a short course. It is recommended that hibernation therapy be used in critically ill patients with oxygenation index <200 mmHg. Artificial hibernation therapy can reduce the body's metabolism and oxygen consumption, and at the same time dilate the blood vessels in the lungs to significantly improve oxygenation. It is recommended to use continuous intravenous bolus injection, and the patient's blood pressure needs to be closely monitored. Use opioids and dexmedetomidine cautiously. Because severe IL-6 levels often cause bloating, opioids should be avoided; 2019-nCoV can still suppress the function of the sinoatrial node and sinus bradycardia occurs, so you should be careful about the heart Inhibiting sedative drugs. In order to prevent the occurrence and exacerbation of lung infections, try to avoid prolonged excessive sedation, and withdrawal of muscle relaxants should be withdrawn as soon as conditions permit. It is recommended to closely monitor the depth of sedation.

8. 氧疗和呼吸支持：① 鼻导管或面罩氧疗，静息吸空气条件下SaO2≤93%，或活动后SaO2＜90%，或氧合指数（PaO2/FiO2）为200～300 mmHg；伴或不伴呼吸窘迫；均推荐持续氧疗。② 经鼻高流量氧疗（high-flow nasal cannula oxygen therapy，HFNC），接受鼻导管或面罩氧疗1～2 h氧合达不到治疗要求，呼吸窘迫无改善；或治疗过程中低氧血症和（或）呼吸窘迫加重；或氧合指数为150～200 mmHg；推荐HFNC。③ 无创正压通气（noninvasive positive pressure ventilation，NPPV），接受HFNC 1～2 h氧合达不到治疗效果，呼吸窘迫无改善；或治疗过程中低氧血症和（或）呼吸窘迫加重；或氧合指数为150～200 mmHg时；可以选用NPPV。④ 有创机械通气，接受HFNC或NPPV治疗1～2 h氧合达不到治疗要求，呼吸窘迫无改善；或治疗过程中低氧血症和（或）呼吸窘迫加重；或氧合指数＜150 mmHg时；应考虑有创通气。首选以小潮气量（4～8 mL/kg理想体质量）为核心的保护性通气策略。

9. ECMO的实施：满足以下条件之一者可考虑实施ECMO。① PaO2/FiO2＜ 50 mmHg超过1 h；② PaO2/FiO2＜80 mmHg超过2 h；③ 动脉血pH值＜7.25并伴有PaCO2＞60 mmHg超过6 h。ECMO模式首选静脉-静脉ECMO。

（四）救治中的特殊问题及处理

1. 糖皮质激素的应用：需谨慎使用糖皮质激素。影像学检查提示肺炎出现明显进展，静息未吸氧状态下患者SaO2≤93%或呼吸急促（呼吸频率≥30次/min）或氧合指数≤300 mmHg，特别是病情进展速度明显加快，面临插管风险时可加用糖皮质激素。患者在插管或ECMO支持可维持有效血氧浓度时，则建议迅速撤退糖皮质激素的使用。对于非

重症患者使用甲泼尼龙，建议剂量控制在20～40 mg/d，重症患者控制在40～80 mg/d，疗程一般为3～6 d。可根据体质量酌量增减。

2. 免疫调节药物的使用：每周2～3次皮下注射胸腺法新，对提高患者免疫功能、阻止病情重症化、缩短排毒时间有一定效果。由于缺乏特异性抗体，目前不支持大剂量使用静脉输注人免疫球蛋白治疗。但部分患者淋巴细胞水平低下，且有合并其他病毒感染的风险，可静脉输注人免疫球蛋白10 g/d，疗程为3～5 d。

3. 合并细菌、真菌感染的精准诊治：对所有重症和危重症患者进行临床微生物监测。每天留取患者痰液和尿液进行培养，高热患者及时行血培养。所有留置血管导管的疑似脓毒症患者，均应同时送检外周静脉血血培养和导管血培养。所有疑似脓毒症患者可考虑采集外周血进行病原学分子诊断检查，包括基于PCR的分子生物学检测及二代测序。

降钙素原水平升高对诊断脓毒症/脓毒性休克具有提示意义。新型冠状病毒肺炎患者病情加重时，存在CRP水平升高，CRP水平升高对诊断细菌和真菌感染引起的脓毒症缺乏特异性。

气道开放的危重型患者后期往往易合并细菌感染和真菌感染。若发生脓毒症，则应尽快给予经验性抗感染治疗。对于脓毒性休克患者，获得病原学诊断前可联合使用经验性抗菌药物，同时覆盖最为常见的肠杆菌科细菌、葡萄球菌和肠球菌感染。住院后发生感染者可选用β内酰胺酶抑制剂复合物。若治疗效果不佳，或患者为重症感染性休克，可换用碳青霉烯类药物治疗。如考虑合并肠球菌和葡萄球菌感染，可加用糖肽类药物（万古霉素）进行经验性治疗，血流感染可选用达托霉素，以肺部感染为主则可选用利奈唑胺。应高度重视危重症患者的导管相关感染，治疗应经验性覆盖甲氧西林耐药的葡萄球菌。可选用糖肽类药物（万古霉素）进行经验性治疗。念珠菌感染在危重症患者中也较为常见，必要时应经验性覆盖念珠菌治疗，可加用棘白菌素类药物。随着重症患者住院时间延长，耐药感染也逐渐增加，此时须根据药物敏感试验调整抗菌药物的使用。

4. 院内感染防控：① 根据2019年国家卫生健康委《医疗机构感染预防与控制基本制度（试行）》，积极推行循证感染防控集束化干预策略，有效预防呼吸机相关肺炎、血管内导管相关血流感染、导尿管相关尿路感染、碳青霉烯耐药革兰阴性杆菌等多重耐药菌和真菌感染。② 严格遵照国家卫生健康委《医疗机构内新型冠状病毒感染预防与控制技术指南(第一版)》《新型冠状病毒感染的肺炎防控中常见医用防护用品使用范围指引(试行)》《新冠肺炎疫情期间医务人员防护技术指南(试行)》的要求，加强流程管理，正确选择和使用口罩、隔离衣、防护服、眼罩、防护面罩、手套等个人防护用品，严格各项消毒隔离措施的落实，最大限度地降低医院感染风险，杜绝医务人员的医院内2019-nCoV感染。

5. 婴幼儿的治疗：轻型患儿仅需对症口服给药治疗。普通型患儿除对症口服给药治疗外，可考虑辨证中药治疗。若合并细菌感染，可加用抗菌药物。重危患儿以对症支持治疗为主，经验给予利巴韦林注射剂抗病毒治疗，15 mg/kg（2次/d），疗程不超过5 d。

（五）中西医结合救治方案

中西医结合救治新型冠状病毒肺炎能提高协同疗效。对于成人患者，通过中医药辨证施治可改善病情。对于轻型患者，证属风热表证者给予中药银翘散加减治疗；以胃肠道症状为主，证属湿遏卫阳者给予藿朴夏苓汤、三仁汤加减。对于普通型患者，证属热邪郁肺者，给予中药麻杏石甘汤加减；证属湿毒郁肺者，给予中药达原饮、甘露消毒丹等加减治疗，可在一定程度上控制病情进展，减少普通型转重型的发生；对于纳差、呕恶、腹胀、乏力、焦虑失眠等，给予中药小柴胡汤加减治疗，可明显改善症状。对于重型患者，如果发热不退，甚至高热、腹胀、粪便干燥闭结，证属热毒闭肺者，给予中药大承气汤灌肠以通腑泻热，使发热减轻或热退，也可用中药白虎汤、升降散和宣白承气汤加减治疗，从而截断病情，减少重型转为危重型的发生。儿童轻型患者，证属时疫犯卫，可用银翘散或香苏散加减。普通型患儿，湿热闭肺者，给予麻杏石甘汤合三仁汤加减；伴腹胀苔腻呕恶等中焦湿热者，可予不换金正气散加减。重型患者若疫毒闭肺（目前全国罕见）可参考成人宣白承气汤合甘露消毒丹加减；若毒热炽盛，腑气不通，食药不下，亦短期予生大黄煎汤灌肠救急。

（六）出院标准

同时符合以下条件者可考虑出院：① 体温恢复正常 > 3 d；② 呼吸道症状明显好转；③ 肺部影像学检查显示急性渗出性病变明显改善；④ 连续两次呼吸道标本核酸检测阴性（采样时间至少间隔1 d）；⑤ 呼吸道标本核酸检测阴性后，粪便病原核酸检测也阴性；⑥ 总病程超过2周。

（七）出院患者的健康管理

1. 对于出院患者，目前仍应密切随访。建议在患者出院后的第2周和第4周至指定的随访门诊进行随访。

2. 患者出院时，应明确其在本市的居住场所和地址。

3. 患者出院后居家休息2周，避免在公共场所活动，必须外出时应佩戴口罩。

4. 根据患者住址(包括宾馆或酒店)，由相关区卫生健康委组织对应医疗机构做好健康管理。2周内专业人员每天2次上门测量患者体温，询问其健康状况，并开展相关健康宣教。

5. If fever and / or respiratory symptoms reappear, the corresponding medical institution should report to the District Health and Health Commission and the District Center for Disease Control and Prevention in a timely manner, and assist in sending them to a designated medical institution within the jurisdiction.

6. After receiving the report, the district health committee and the district disease prevention and control center shall report to the superior department in time.

Conflict of interest All authors declare that there is no conflict of interest

References slightly

Read more