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# Clinical characteristics and remission of nine cases with coronavirus disease 2019 infection in Zunyi, Southwest of China

## A retrospective study

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**Abstract**

The outbreak of coronavirus disease 2019 (COVID-19) has become a rock-ribbed public pandemic and caused substantial health concerns worldwide. In addition to therapeutic strategies, the epidemiologic features and clinical characteristics of patients responded to COVID-19 infection are of equal importance. The study aims to systematically evaluate the clinical presentations and remission of cases with COVID-19 infection in Zunyi, Southwest of China, and to determine the similarities and variations for further clinical classification and comprehensive treatment. Herein, we conducted a retrospective study upon 9 patients in Zunyi, southwest of China, including 1 mild (LPA), 5 severe (SPA) and 3 critical (CPA) types of COVID-19 infection. In details, the demographic data, historical epidemiology, previous medical history, clinical symptoms and complications, laboratory examination, chest imaging, treatment and outcomes of the patients were throughout explored. The non-normal distribution of the data was conducted by utilizing the SPSS software, and significant statistical differences were identified when $P < .05$. By retrospective analysis of the 9 cases, we found there were multifaceted similarities and differences among them in clinical representation. The patients collectively showed negative for nucleic acid test (NAT) and favorable prognosis after receiving comprehensive therapy such as hormonotherapy, hemopruification, and antiviral administration as well as respiratory support. On the basis of the information, we systematically dissected the clinical features and outcomes of the enrolled patients with COVID-19 and the accompanied multiple syndromes, which would serve as new references for clinical classification and comprehensive treatment. Analysis of clinical characteristics and therapeutic effect of 9 cases of novel coronavirus pneumonia (COVID-19), ChiCTR2000031930. Registered April 15, 2020 (retrospective registration).

**Abbreviations:** COVID-19 = coronavirus disease 2019, NAT = nucleic acid test, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2, SOFA = sequential organ failure assessment.

**Keywords:** clinical classification, COVID-19, hemopurification, mechanical ventilation, multiple complications

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*The patients signed informed consents to the publication of their reports.*

*The authors have no conflicts of interest to disclose.*

*The datasets generated during and/or analyzed during the current study are publicly available.*

*The research followed the declaration of Helsink and internationally recognized guidelines. Meanwhile, ethical approval of the research was signed by the ethical Committee of Affiliated Hospital of Zunyi Medical University in China (approval number: KLL-2020-013).*

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## 1. Introduction

The outbreak of coronavirus disease 2019 (COVID-19) pandemic induced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has infected >59.1 million people and caused nearly 1.4 million deaths worldwide according to the statistical data of Johns Hopkins Coronavirus Resource Center (https://coronavirus.jhu.edu/map.html). Initially, the first four documented cases with "pneumonia of unknown etiology" were identified and reported by local hospitals on December 29, 2019 in Huanan Seafood Wholesale Market, Wuhan, Hubei province of China.[1] Soon after, the disorder was identified with human-to-human transmission characteristics based on demographic features, exposure history, clinical presentations and laboratory examination in accordance with Centers for Disease Control and Prevention guidelines and WHO (World Health Organization) recommendation.[1–3] In general, most of the cases with the spectrum of clinical symptoms, such as fever, headache, dry cough, rhinorrhea, fatigue, nausea, vomiting, diarrhea, abdominal discomfort, and bilateral ground-glass opacities in lungs, together with multiple complications in lower airway and lungs.[3,4] Meanwhile, a certain number of cases were reported with multiple complications such as diabetes, hypertension, cardiovascular diseases, which further contributed to the complexity of classification of disease diagnosis and the treatment.[5,6] Worse still, the elderly patients were reported with higher morbidity and mortality rates and worse prognosis mainly due to the lower levels of immunity, increasingly inflammatory cytokine storm, as well as the COVID-19 pneumonia-induced acute lung injury and acute respiratory distress syndrome and even the multiple system organ failure.[1,5]

Meanwhile, considerable efforts have been synchronously made to reduce transmission and improve outcomes of patients with COVID-19 infection. On the one hand, policy interventions have been carried out based on the rationale of 3-14 days of latentperiod and droplet transmission, such as prohibited gathering and wear facemarks in public places, large-scale nucleic acid screening, trajectory tracking and home quarantine, which have been proved with splendid efficacy for COVID-19 blockade.[3,7] On the other hand, comprehensive treatment and care have been developed for remission of intolerable illness and help improve the outcomes of the patients. To date, numerous clinical trials involved the antiviral drugs, neutralizing antibodies and antibiotics, anti-inflammatory corticosteroids, immunotherapeutics, Chinese medicine, telemedicine, gastric mucosal protection, and supportive therapeutics, and in particular, the forthcoming clinical grade vaccines and cell therapy.[8–16] For instance, we and other investigators reported the efficacious remission of elderly patients with COVID-19 infection and multiple comorbidities with the aid of systemic administration of mesenchymal stem/Stromal cells, respectively.[12,17] It's noteworthy that Market and the colleagues outlined recommendations for natural killer (NK) cell-based therapeutic strategies against COVID-19 in clearing the virus and preventing the potential damage of immunopathological responses.[18] However, most of the current studies intensively focused on epidemiology, etiology, genomics and outcomes of COVID-19 infection, yet the systematic and meticulous dissection of the detailed information upon clinical characteristics and outcomes with diverse disease classification remains caliginous and unavailable.[19–21]

In this study, we conducted a retrospective study upon 9 patients with COVID-19 infection in Zunyi, southwest of China. Of the enrolled cases, 1 was mild type, 5 were severe type and remaining 3 were critical ill type, and all of them were discharged from hospital with recovery after comprehensive therapy. By systematic analysis, we summarized the general information of the patients including demographic and clinical characteristics, laboratory tests together with the outcomes, which would benefit the clinical classification and optimal treatment study of COVID-19.

## 2. Methods

### 2.1. Ethical approval

The experiment on the patients followed the internationally recognized guidelines and principles of the Declaration of Helsinki. Ethical approval of the research was approved by the Ethical Committee of Affiliated Hospital of Zunyi Medical University in China (approval number: KLL-2020-013). The 9 patients signed informed consents to the publication of their reports.

### 2.2. Data collection

The information of the enrolled 9 cases in the Department of Intensive Care Unit (ICU) were collected from the Electronics Medical Records (EMR) management system with the consents of the patients and ethical committee, including the demographic data, epidemiological history, past medical history, clinical symptoms and vital signs, laboratory tests, chest radiology, therapeutic options and outcomes. The definite diagnosis and classification of the patients was according to the fifth version of Guidelines of Diagnosis and Treatment Options for COVID-19 released by the National Health Commission of the People's Republic of China.

### 2.3. Laboratory examination

The COVID-19 associated laboratory examinations were conducted according to the guidelines of Chinese Centers for Disease Control and Prevention and WHO recommendations as previously reported.[1] The RNAs in the rhinal and respiratory tract specimens were collected and extracted from the 9 cases for SARS-CoV-2 nuclei acid test (NAT) by utilizing the standard quantitative real-time reverse transcription-polymerase chain reaction.

### 2.4. Statistical analysis

The non-normal distribution of the data was analyzed by utilizing the quartile and percentile statistical description methods and SPSS 25.0 software (IBM). The other statistical analyses were conducted by GraphPad Prism 6.0 (GraphPad, San Diego, CA) Software as we described before.[22–25] Statistically significance was confirmed between the 2 groups when $P$ value was <.05 ($P < .05$). All data were shown as mean ± SD. $*P < .05$; $**P < .01$; $***P < .001$; $****P < .0001$; NS, not significant.

## 3. Results

### 3.1. General information

During January 30th, 2020 and June 4th, 2020, the Department of Intensive Care Unit (ICU) of Affiliated Hospital of Zunyi Medical University in China enrolled 9 cases with COVID-19 infection, including 5 males and 4 females. Of them, 2 cases with diabetes, while one ninth patient with chronic obstructive pulmonary disease, coronary heart disease or malignant tumor instead. Beside the major clinical symptoms of COVID-19 (e.g., fever, cough, weak, headache and nausea), a certain number of cases with complications such as myocardial damage, acute kidney injury, acute liver injury, pneumothorax and shock. According to the fifth version of Guidelines of Diagnosis and Treatment Options for COVID-19, 1 case was diagnosed with mild type (LPA), 5 cases and 3 cases were diagnosed with severe (SPA) and critical (CPA) types, respectively. All of them showed typical ground-glass opacity and inflammatory exudate in the lung to varying degrees, thus overall received antiviral and antibiotics treatment, and a majority of them simultaneously received thymalfasin, hormone and hemopurification together with respiratory support including high flow

oxygen therapy and oxygen uptake as well (Supplemental digital Digital Content Table 1, http://links.lww.com/MD/H784, Fig. 1A–C).

### 3.2. Clinical characteristics and laboratory tests

Ulteriorly, laboratory tests indicated that all cases showed decline in total lymphocytes (LYMPH%) but with normal platelet content in the peripheral blood (Supplemental digital Digital Content Table 2, http://links.lww.com/MD/H785).

According to routine blood test, a proportion of 66.7% patients revealed upregulated level of c-reactive protein (CRP). Simultaneously, 77.88% and 88.89% of the cases showed elevated levels of proinflammatory factors IL-6 and IL-10, respectively. As to respiratory-associated parameters, a percentage of 77.78% and 100% of the enrolled patients with 50% fraction of inspiration O2 (FiO2), lactic acid (LAC ≥ 1.5 mmol/L), and oxygenation index (OI ≤ 300 mm Hg), respectively.

To further dissect the potential similarities and differences, systemic laboratory tests were conducted upon the enrolled patients with mild (SPA), severe (SPA) and critical (CPA) types of COVID-19 infection. According to the blood gas assay, the patients in the indicated groups showed similarities in multiple physical signs such as FiO2, OI and partial pressure of oxygen (pO2), but with enhanced FiO2 in the CPA group (Fig. 2A, Supplemental digital Digital Content Fig. 1A, http://links.lww.com/MD/H789).

Even though with further decreasing tendency in multiple blood constituents (e.g., WBC, LYMPH%, PLT) in the CPA group compared with the SPA cases, yet no statistically significant differences were observed (Fig. 2B). Conversely, a gradually upward tendency of biochemical indexes, including lactate dehydrogenase (LDH) with statistical differences or CRP, procalcitonin (PCT), total bilirubin (TBiL) and serum creatinine (SCR), in SPA and CPA patients were noticed (Fig. 2C, Supplemental digital Digital Content Fig. 1B, http://links.lww.com/MD/H789).

As expected, in accordance with the increases of the severity of the COVID-19 classification, the secretory IL-6 and IL-10 in peripheral blood of patients were collectively increased compared with the healthy donors (negative controls, NC). Interestingly, the CPA cases manifested the highest levels of multiple inflammatory factor expression (IL-2,

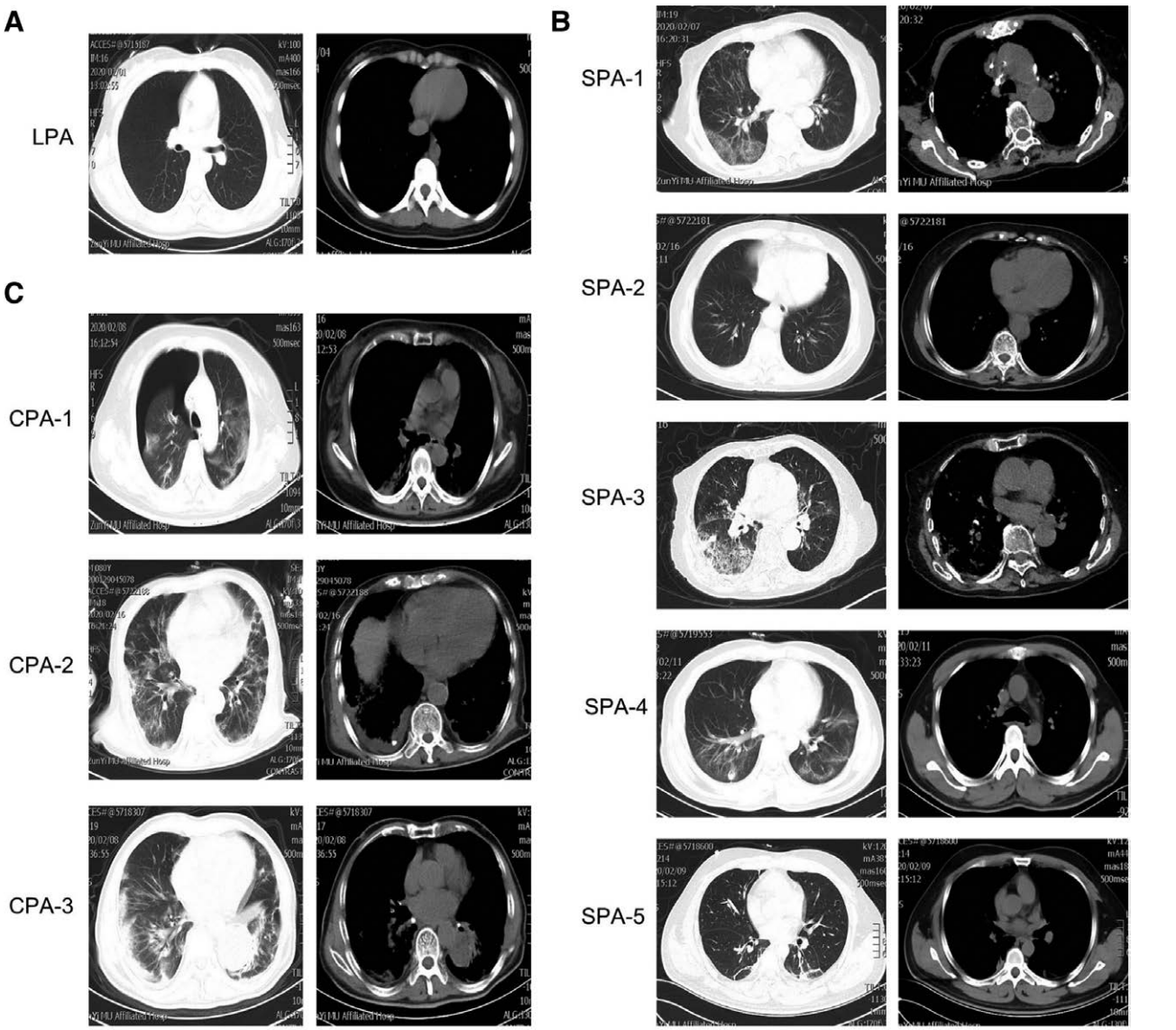


**Figure 1.** The chest radiographs of 9 patients with COVID-19 infection. (A–C) The chest X-ray images of the patients with COVID-19 infection, including one with mild infection (A), 5 with severe infection (B), and 3 with critical ill infection (C). COVID-19 = Coronavirus Disease 2019.

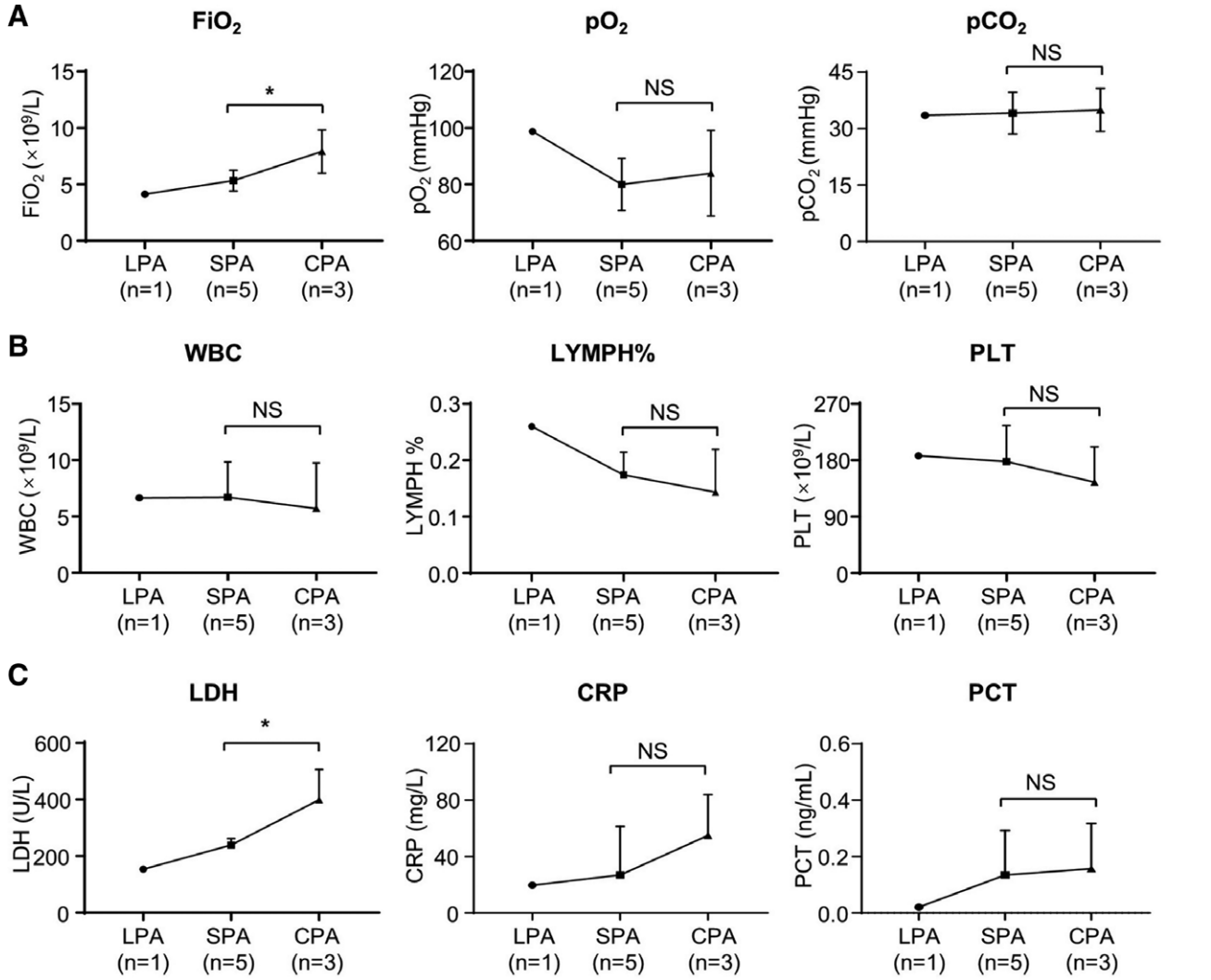


**Figure 2.** The dynamic variations of clinical parameters in 9 patients with COVID-19 infection. (A) The variations of FiO2 value, PO2 value, pCO2 value in the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. (B) The variations of WBC ($10^9$/L), LYMPH (%) and PLT ($10^9$/L) in the peripheral blood of the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. (C) The variations of LDH (U/L) value, CRP (mg/L) value, PCT (ng/mL) value in the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. COVID-19 = Coronavirus Disease 2019.

IL-4, TNF-α, IFN-γ) compared with those in the LPA and CPA groups (Fig. 3A). Nevertheless, the levels of the abovementioned proinflammatory-associated cytokines in the 9 patients (PA) were significantly higher than those in the NC groups (Fig. 3B).

### *3.3. Clinical outcomes*

In general, with the aid of the aforementioned comprehensive treatment, all of the enrolled patients in ICU were safely discharged without death. In details, the range of sequential organ failure assessment (SOFA) scores was between 8 and 11 with a median of 9. The days of NAT negative, in ICU and hospital for all cases were 11.5 to 21.5 (median: 12), 8.5 to 16.5 (median: 14), and 8.5 to 16.5 (median: 14), respectively (Supplemental digital Digital Content Table 3, http://links.lww.com/MD/H786).

Furthermore, from the view of multiple prognosis-correlative curves, we confirmed the consistency of disease scores and outcomes of the patients in the aforementioned groups, including the SOFA, days for SARS-CoV-2 NAT negative, in ICU and in hospital (Fig. 4A–D, Supplemental digital Digital Content Table 4, http://links.lww.com/MD/H787).

For the purpose of systematically evaluating the efficacy of comprehensive therapy upon COVID-19 infection, the multifaceted clinical parameters were compared detail by detail before (before PA) and after (after PA) recovery. Opposite to the tendency of FiO2 variation, pO2 value other than pCO2 value showed remarkable upregulation after recovery (Fig. 5A, Supplemental digital Digital Content Fig. 2A, http://links.lww.com/MD/H790).

Consistently, compared with the previous morbid state, the content of total lymphocytes (LYMPH) in peripheral blood manifested moderate elevation, whereas no statistically significant differences were observed in other counterparts (Fig. 5B, Supplemental digital Digital Content Fig. 2B, http://links.lww.com/MD/H790). Furthermore, to assess the potent variations, we verified the sharply decreased cytokine storm-associated proinflammatory factors such as IL-4, IL-6, IL-10, TNF-α and TNF-γ in the COVID-19 patients after comprehensive treatment (Fig. 5C, Supplemental digital Digital Content Fig. 2C, http://links.lww.com/MD/H790).

In the meantime, except for other clinical indicators, the expression levels of liver-associated aspartate aminotransferase (AST) and albumin (ALB), heart-associated brain natriuretic peptide and kidney-associated blood urea

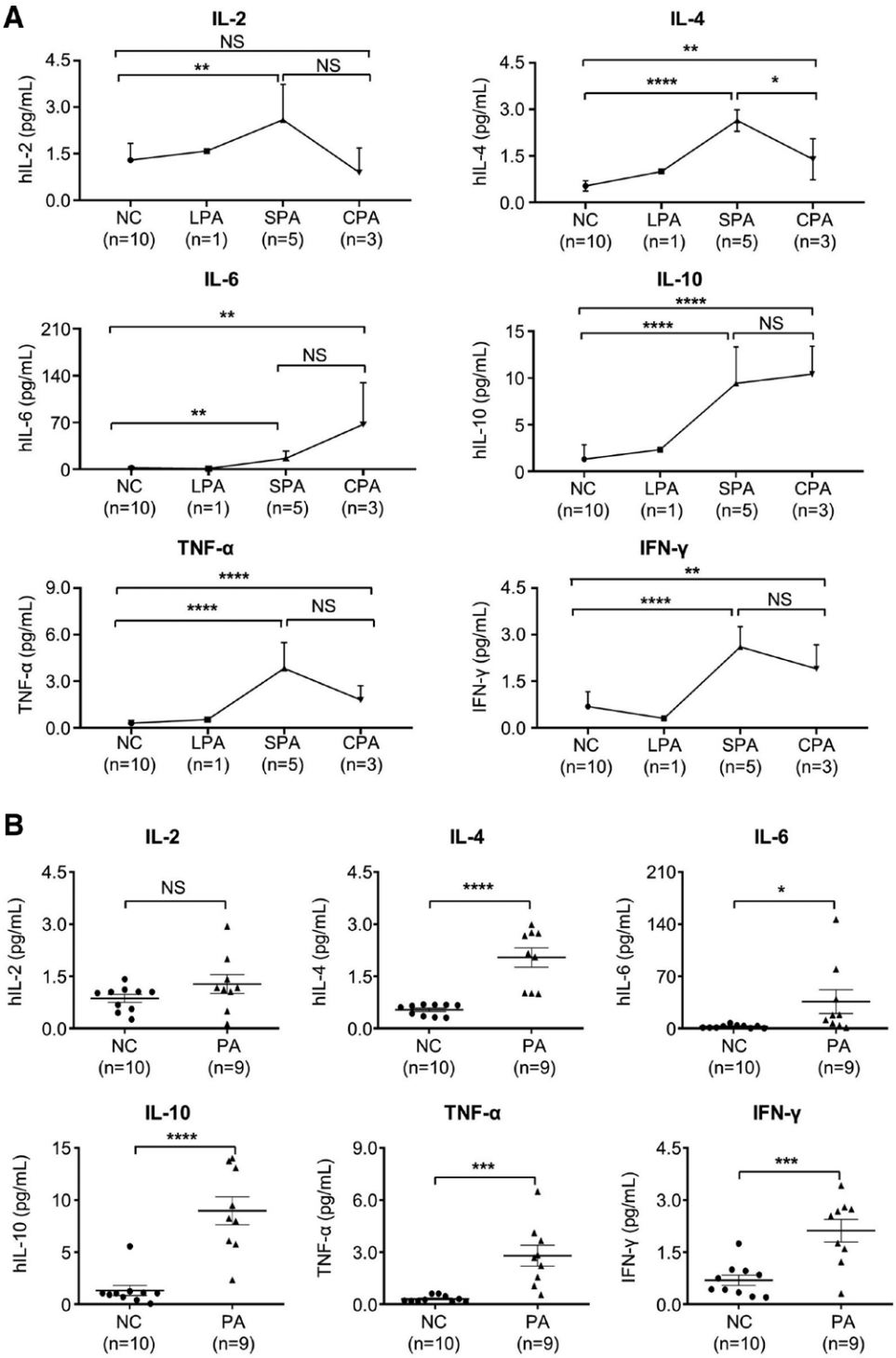


**Figure 3.** The variations of clinical parameters in 9 patients with COVID-19 infection. (A) The variations of IL-2 (pg/mL), IL-4 (pg/mL), IL-6 (pg/mL), IL-10 (pg/mL), TNF-α (pg/mL), INF-γ (pg/mL) in the peripheral blood of the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. (B) The variations of IL-2 (pg/mL), IL-4 (pg/mL), IL-6 (pg/mL), IL-10 (pg/mL), TNF-α (pg/mL), INF-γ (pg/mL) in the peripheral blood of health donors (NC) and the patients with COVID-19 infection (PA).

nitrogen biomarkers were moderately recovered after comprehensive treatment (Fig. 5D and E, Supplemental digital Digital Content Fig. 2D and E, http://links.lww.com/MD/H790, Supplemental digital Digital Content Tables 5 and 6, http://links.lww.com/MD/H788). Collectively, these results suggested the effectively remission and clinical outcomes of multiple organ dysfunction syndrome and the accompanied multiple comorbidities.

## 4. Discussion

Current studies have enlightened the epidemiology, etiology, duration of human transmission and therapeutic strategies of COVID-19, yet the systematical and detailed information of the disorder still needs to be further fulfilled by future exploration.[3,4] In this study, we reported a cohort of 9 patients with laboratory-confirmed COVID-19 infection and required ICU admission in Affiliated Hospital of Zunyi Medical University,

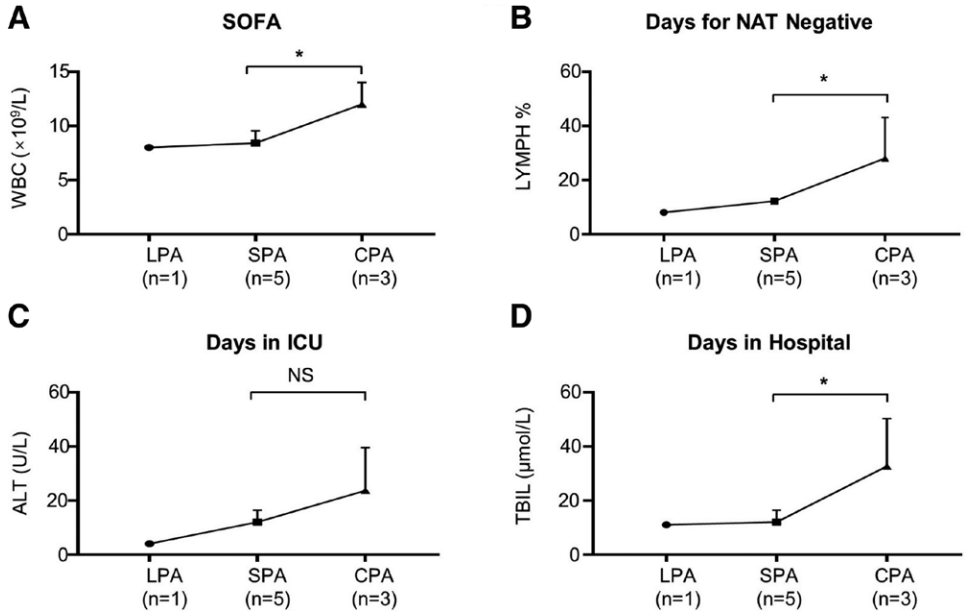


**Figure 4.** The variations of clinical parameters in healthy donors (NC) and 9 patients with COVID-19 infection (PA). (A) The variation of severity of illness-associated indicators including the standard SOFA value in the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. (B–D) The variations of days negative for nucleic acid testing (NAT) (B), days in ICU (C), days in hospital (D) among the patients with mild (LPA), severe (SPA) or critical ill (CPA) infection. COVID-19 = Coronavirus Disease 2019, SOFA = sequential organ failure assessment.

Guizhou province of China. The clinical presentations of the cases were retrospectively analyzed from the view of disease classification and longitudinal follow-up. Strikingly, with the aid of ICU and comprehensive administration, all of the cases with multidimensional variations in clinical characteristics collectively came into rehabilitation without death.

During the past 2 decades, disease-causing culprits such as coronaviruses with enveloped non-segmented RNAs have resulted in several global pandemics, including the life-threatening Middle East respiratory syndrome coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus (SARS-CoV).[6,26] Distinguish from the indicated 2 β coronaviruses, the SARS-CoV-2 caused lower mortality rates but with more rapid human-to-human attributes and clusters of acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).[27,28] State-of-the-art renewal indicated the major pathogenic pattern of SARS-CoV-2 by binding to the angiotensin I converting enzyme 2 expressed in the host alveolar epithelial cells and capillary endothelial cells.[12,29–31] In this study, we observed that SARS-CoV-2 didn't cause significant increase in the permeability of alveolar epithelial cells, thus adequate attentions should be paid to the destruction of the pulmonary capillary endothelial cell barrier. In our view, the reasons for rapid damage of lung tissues in advanced stage of COVID-19 infection might mainly including 2 aspects. Firstly, the high viral load in lung tissue led to the large scale pulmonary capillary endothelial cell infection and attack by the host immune cells; Secondly, the accompanied inflammatory cytokine storm and acute lung injury and acute respiratory distress syndrome caused more serious secondary damage to the local lung tissue.[30,32,33] Herein, we further noted that patients with more severe type of COVID-19 showed worse blood gas indexes, lower total lymphocytes, and higher levels of T-helper-2 (Th2) secreted cytokines (e.g., IL-4, IL-10) and relevant proinflammatories (e.g., IL-6, TNF-α, IFN-γ) compared with those in the mild type group, which manifested the positive association between cytokine storm and the resultant disease severity. Interestingly, we also noticed that there were no statistically significant differences between the SPA and CPA groups, which might due to the status of sufficient deterioration and the individual differences. However, we did verify the prolonged duration in ICU and hospital together with the higher SOFA score. Taken together, our findings added new references to help elucidate the pathogenesis and outline the clinical profiles of COVID-19.

On the basis of fundamental and clinical research, a certain number of therapeutic options have been developed.[13,17,18,30] For instance, Lopinavir and Ritonavir showed antivirus activity upon MERS-CoV and SARS-CoV-2 in nonrandomized trials by targeting the RdRp site, which effectively suppressed the replication and transcription process. Interferon (IFN) was competent for binding to activate and synthesize the antiviral protein coding genes.[30] However, the employ of proinflammatory factor antibodies might cause non-effective therapy upon the cytokine storm attributes to the potential cascades of adverse reactions.[10,11] In this study, we noted the perfect correlation of secreted IL-6 with the severity and outcomes of the 9 cases, which was much reliable to the CRP value and could be effectively eliminated with other inflammatory cytokines and chemokines by hemopurification based on the physical properties of molecular weight between 10KD and 30KD.[34] Therefore, we conducted hemopurification and transnasal hyperflow oxygen therapy (HFNC) in 3 cases with abnormally increased oxygen concentration caused by the severe cytokine storm, and all of them showed remission in oxygen concentration and negative NAT, which was consist with Lee's artificial liver therapy upon cytokine storm. Taken together, comprehensive therapy, including broad-spectrum antiviral therapy, respiratory support, and early hemopurification and cytokine storm removal, are effective measures for severe/critically ill COVID-19 patients to pass the crisis.[14,35] Meanwhile, we realized that this study is a single-center report, and the conclusions still needs further large-scale confirmation.[5] Therefore, clinicians should make all-around treatment options based on patients' clinical manifestations, vital signs, laboratory examination and imaging examination as well.

## 5. Conclusions

Overall, with the aid of a systematically and meticulously retrospective review, we identified the multifaceted similarities and

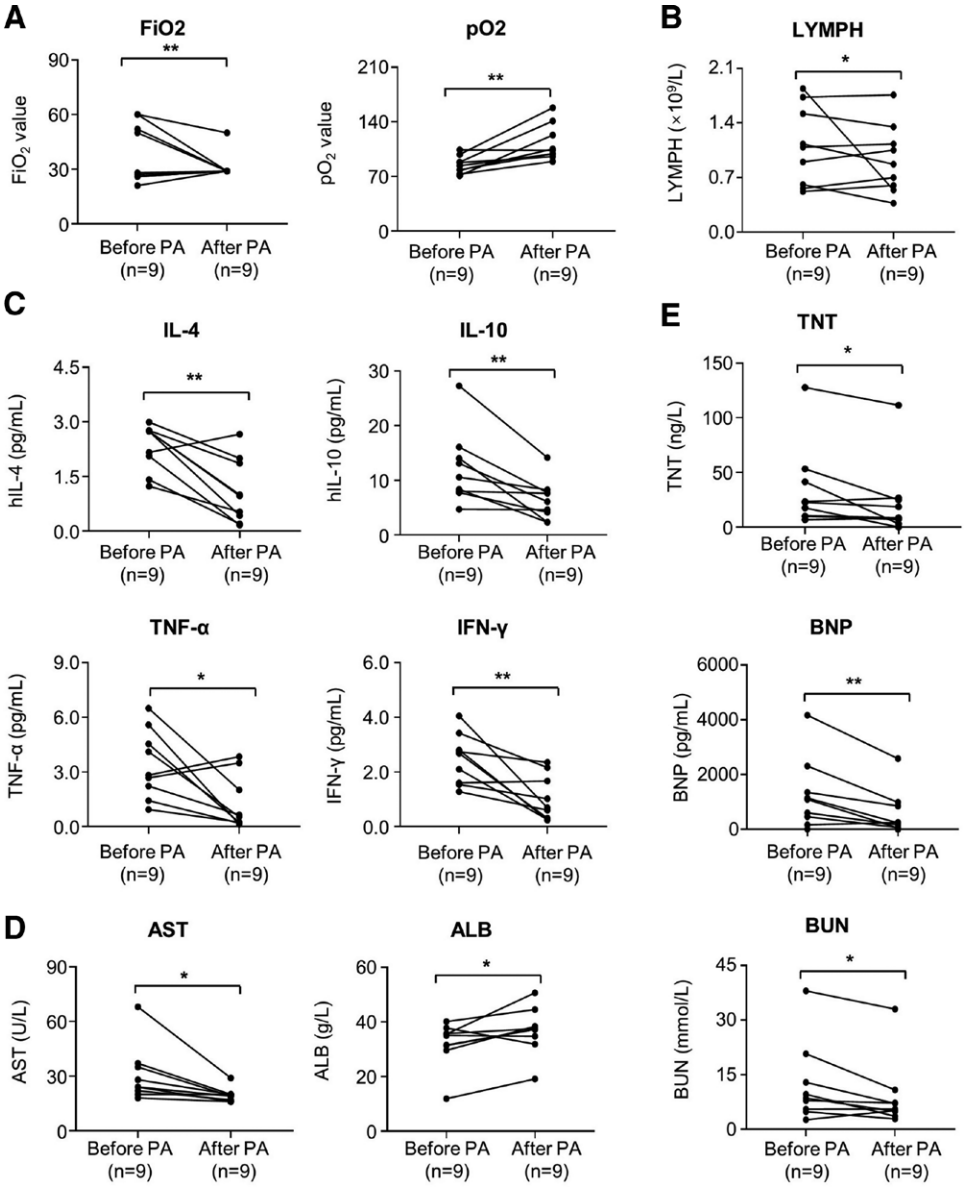


Figure 5. The variations of clinical parameters in the 9 patients before treatment (Before PA) and after recovery (After PA). (A) The variations of FiO2 value, $PO_2$ value in the patients before treatment (Before PA) and after recovery (After PA). (B-D) The variations of LYMPH ($10^9$/L) (B), IL-4 (pg/mL), IL-10 (pg/mL), TNF-α (pg/mL), INF-γ (pg/mL) (C), AST (U/L) and ALB (g/L) (D) in the peripheral blood of the patients before treatment (Before PA) and after recovery (After PA). (E) The variations of TNT (ng/L), BNP (pg/mL), and BUN value in the peripheral blood of the patients before treatment (Before PA) and after recovery (After PA). BNP = brain natriuretic peptide, BUN = blood urea nitrogen.

differences in epidemiologic and clinical characteristics as well as outcomes of 9 patients in Zunyi, Southwest of China with COVID-19 infection. Our findings would serve as new references for clinical classification and comprehensive treatment of COVID-19.

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## Author contributions

Hongjun Chen, Miao Chen: collection and assembly of data, manuscript writing; Wei Zhang, Zhihua Dai: collection and assembly of data; Hongjun Chen and Leisheng Zhang: interpretation, manuscript writing and revision;Yiyong Wei and Miao Chen: conception and design, data analysis, final approval of manuscript.
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**Writing – review & editing:** Yiyong Wei, Miao Chen.

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