CONVALESCENT PLASMA FOR TREATMENT OF COVID-19 (UPDATE)

Based on available evidence up to 28 August 2020

INTRODUCTION

Convalescent plasma (CP) therapy, a classic adaptive immunotherapy, also known as passive antibody therapy, has been applied to the prevention and treatment of many infectious diseases for more than one century. Convalescent plasma therapy was successfully used in the treatment of SARS1, MERS, and 2009 H1N1 pandemic with satisfactory efficacy and safety.[2]

Amid testing the already existing antiviral drugs and new ones, the researchers have come across the CP therapy, which could be a potential treatment for the virus. Several countries including China and the US have already started the clinical trials of the convalescent plasma therapy due to the absence of a coronavirus-specific treatment to cure the infected patients.[2,3,4]

To date, no specific treatment was recommended for SARS-CoV-2 / COVID-19 infection except for meticulous supportive care and CP therapy has not yet been approved for use by the US Food and Drug Administration (FDA), so it is regulated as an investigational product. The USFDA is also facilitating access to COVID-19 convalescent plasma for use in patients with serious or immediately life-threatening COVID-19 infections through the process of Single Patient Emergency Investigational New Drug (IND). Health care providers may want to consider patient eligibility and donor eligibility before emergency use of COVID-19 CP to treat patients.[5]

EVIDENCE

There were 25 articles retrieved from the scientific databases such as Medline, EBM Reviews, EMBASE via OVID, PubMed, the general search engines [Google Scholar and US Food and Drug Administration (USFDA)] using the keywords of *"convalescent plasma"*, *"coronavirus"* and *"COVID-19"*. Nine relevant articles were included in this review.

Duan K et al. (2020) conducted a pilot case control study in three participating hospitals in China. In this study, ten severe patients (n=10) from January 23, 2020, to February 19, 2020 (six males and four females) were enrolled and received CP transfusion. None of the patients had direct exposure to the Huanan Seafood Wholesale Market. All patients were confirmed by real-time viral RNA tests and received one dose of 200 mL of convalescent plasma (CP) derived from recently recovered donors with the neutralizing antibody titers above 1:640. The CP therapy was transfused to the patients as an addition to maximal supportive care and antiviral agents. Nine patients received arbidol monotherapy or combination therapy with remdesivir or ribavirin or peramivir, while one patient received ribavirin monotherapy.

Antibacterial or antifungal treatment was used when patients had co-infection. Six patients received intravenous (i.v.) methylprednisolone (20 mg every 24 h). A computerized tomography investigation showed that all patients presented with bilateral ground-glass opacity and/or pulmonary parenchymal consolidation with predominantly subpleural and bronchovascular bundles distribution in the lungs. Seven patients had multiple lobe involvement, and four patients had interlobular septal thickening.[2]

All clinical symptoms in the ten patients, especially fever, cough, shortness of breath, and chest pain, disappeared or significantly improved within Day 1 to Day 3 upon CP transfusion. Two patients were able to wean off from mechanical ventilation to high-flow nasal cannula, and one patient discontinued high-flow nasal cannula after receiving CP. Lymphocytopaenia, an important index for prognosis in COVID-19, tended to be improved after CP transfusion (median: 0.65 × 109 per L vs. 0.76 × 109 per L) with seven out of 10 patients showing an increase of lymphocyte counts. Several other parameters tended to improve as compared to pre-transfusion, including increased lymphocyte counts (0.65 × 109 /L vs. 0.76 × 109 /L) and decreased C-reactive protein (55.98 mg/L vs. 18.13 mg/L). Radiological imaging showed varying degrees of absorption of lung lesions within seven days in reduction of pulmonary lesions on chest CT. There were no serious adverse reactions or safety events recorded after CP transfusion.[2]

The study also compared a historic control group of ten (n=10) patients which was randomly selected from the cohort treated in the same hospitals and matched by age, gender, and severity of the diseases. Baseline characteristics of patients between CP treatment group and control group showed no significant differences, while clinical outcomes of these two groups were different. Three cases were discharged while seven cases were in much improved status and ready for discharge in CP group, as compared to three deaths, six cases in stabilised status, and one case in improvement in the control group ($p < 0.001$).[2]

The authors concluded that this pilot study on CP therapy shows a potential therapeutic effect and low risk in the treatment of severe COVID-19 patients. One dose of CP with a high concentration of neutralising antibodies can rapidly reduce the viral load and tends to improve clinical outcomes. The optimal dose and treatment time point, as well as the definite clinical benefits of CP therapy, need to be further investigated in randomised clinical studies.[2]

Shen C et al. (2020) reported their clinical experience in a case series of five critically ill COVID-19 patients treated with convalescent plasma transfusion in Shenzhen Third People's Hospital, China. All patients presented with acute respiratory distress syndrome (ARDS) and met these three following criteria: 1) severe pneumonia with rapid progression and continuously high viral load despite antiviral treatment; 2) PAO2/FIO2<300; and 3) requiring mechanical ventilation. Each patient received two consecutive transfusions of 200 to 250 mL of ABO-compatible convalescent plasma (400 mL of convalescent plasma in total) on the same day it was obtained from the donor. Convalescent plasma was administered between 10 and 22 days after admission. The patients also received antiviral agents (*combination of two or three of these drugs : lopinavir/ritonavir; interferon alfa-1b; favipiravir; arbidol; darunavir*) continuously until the SARS-CoV-2 viral loads became negative. **Following plasma**

transfusion, body temperature normalised within three days (4 of 5 patients), the SOFA score decreased, and PAO2/FIO2 increased within 12 days. Viral loads decreased and tested negative within 12 days after the transfusion. SARS-CoV-2–specific ELISA and neutralizing antibody titers increased following the transfusion. Clinically, ARDS resolved in four patients at 12 days after transfusion, and three patients were weaned from mechanical ventilation within two weeks of treatment. Of the five patients, three have been discharged from the hospital (length of stay: 51 to 55 days), and two were in stable condition at 37 days after transfusion. The authors concluded that administration of convalescent plasma containing neutralizing antibodies may improve the clinical conditions of critically ill COVID-19 patients with ARDS. However, the limited sample size and study design preclude a definitive statement about the potential effectiveness of this treatment, and these observations require evaluation in clinical trials.[6]

Hartman W et al. (2020) conducted a cross sectional study that was approved by the University of Wisconsin Institutional Review Board in the United States. Thirty-one treated-patients were involved, 16 severe patients and 15 life-threatened patients as measured by Sequential Organ Failure Assessment scores. All appropriate regulatory, Institutional Review Board and patient care protocols were in place to begin transfusions by April 9, 2020. The first unit from donor screening program was collected on April 10, 2020 with acceptable units available for patient transfusion on April 12, 2020.[7]

Overall mortality was 27% (4/31) but only patients with life-threatening disease died. Around 94% of transfused patients with severe disease avoided escalation to ICU care and mechanical ventilation and 67% of patients with life-threatening disease were able to be extubated. Most transfused patients had a rapid decrease in their respiratory support requirements on or about day 7 following convalescent plasma transfusion. The authors concluded the results demonstrate that convalescent plasma is associated with reducing ventilatory requirements in patients with both severe and life-threatening disease, but appears to be most beneficial when administered early in the course of disease when patients meet the criteria for severe illness.[7]

Abolghasemi H et al. (2020) conducted a non-randomised clinical trial study in seven participating hospitals in Iran between March to April 2020 involving 189 patients (115 convalescent plasma treatment group and 74 control group). Patients were recruited from confirmed COVID-19 infected patients which were confirmed by quantitative real time polymerase chain reaction (q-RTPCR) on their admission to the hospital. All patients in the case and control groups received similar routine antiviral therapy including Lopinavir/Ritonavir, Hydroxychloroquine, and an anti-inflammatory agent.[8]

Table 1 shows comparison of outcomes including all-cause mortality, total hospitalisation days and needs for intubation between the two patients' groups. A total of 98 (98.2 %) patients who received convalescent plasma were discharged from hospital which is substantially higher compared to 56 (78.7 %) patients in control group. Length of hospital stay was significantly lower (9.54 days) in convalescent plasma group compared with that of control group (12.88 days). Only eight patients (7%) in convalescent plasma group required intubation while this value was 20 % in control group. No adverse effect was observed resulting from convalescent plasma transfusion during the study.[8]

Table 1: Comparison of primary and secondary outcomes between the two groups.[8]

Outcome		Patient groups		p-value
		Plasma (n = 115)	Control (n = 74)	
All-cause mortality	Died, (n; %)	17 (14.8 %)	18 (24.3 %)	0.09
	Alive, (n; %)	98 (85.2 %)	56 (75.7 %)	
Length of stay, day[1]	Mean ± SD	9.54 ± 5.07	12.88 ± 7.19	0.002
	Range	2–24	2–32	
Length of stay, day[2]	Mean ± SD	6.25 ± 4.33	12.88 ± 7.19	0.000
	Range	0–20	2–32	
Patients discharged from hospital ≤5 days post admission	n (%)	27 (28.1 %)	5 (8.9 %)	0.010
Intubation	No, (n; %)	107 (93 %)	59 (79.7 %)	0.006
	Yes, (n; %)	8 (7.0 %)	15 (20.3 %)	

[1]Total hospital stay based on 1st day of hospital admission.
[2]Total hospital stay based on 1st day of convalescent plasma transfusion.

The authors concluded that this non-randomised clinical trial presented here demonstrates the clinical efficacy of convalescent plasma in COVID-19 infected patients and indicates that convalescent plasma treatment should be considered as an effective and safe therapy for COVID-19 patients. Convalescent plasma therapy substantially improved patients' survival, significantly reduced hospitalization period and needs for intubation in COVID-19 patients in comparison with control group. [8]

Joyner M et al. (2020) conducted a case series study from April 3 to May 11, 2020, in analysing key safety metrics after transfusion of ABO-compatible human COVID-19 convalescent plasma in 5,000 hospitalized adults with severe or life-threatening COVID-19, with 66% in the intensive care unit, as part of the US FDA Expanded Access Program for COVID-19 convalescent plasma. At the time of enrollment, 4,051 (81%) patients had severe or life-threatening COVID-19 and 949 (19%) were judged to have a high risk of progressing to severe or life-threatening COVID-19. Prior to COVID-19 convalescent plasma transfusion, a total of 3,316 patients (66%) were admitted to the ICU. Of the 4,051 patients diagnosed with severe or life-threatening COVID-19.[9]

Within four hours of completion of the COVID-19 convalescent plasma transfusion (inclusive of the plasma transfusion), 36 serious adverse events (SAEs) were reported (<1% of all transfusions). The attribution scale used by the treating physicians for evaluating the SAEs included unrelated, possibility related, probably related, or definitely related. Of the SAEs, 15 deaths were reported (0.3% of all transfusions) and four of those deaths were judged as related (possibly, n=3; probably, n=1; definitely, n=0) to the transfusion of COVID-19 convalescent plasma. There were 21 non-death SAEs reported, with seven reports of transfusion associated circulatory overload (TACO), eleven reports of transfusion-related acute lung injury (TRALI), and three reports of severe allergic transfusion reaction. All incidences of TACO and TRALI were judged as related (possibly, n=9; probably, n=7; definitely, n=2) to the transfusion of COVID-19 convalescent plasma.[9] The SAEs and their attributions are summarized in Table 2.

Table 2: Serious Adverse Event (SAE) Characteristics.[9] (n=5000)

Four Hour Reports	Reported *(n = 36)*	Related[a] *(n = 25)*	Estimate (95% CI)
Mortality	15	4	0.08% (0.03%, 0.21%)
Transfusion-Associated Circulatory Overload (TACO)	7	7	0.14% (0.07%, 0.29%)
Transfusion-Related Acute Lung Injury (TRALI)	11	11	0.22% (0.12%, 0.39%)
Severe allergic transfusion reaction	3	3	0.06% (0.02%, 0.18%)
Seven Day Reports	**Reported**		**Estimate (95% CI)[b]**
Mortality	602		14.9% (13.8%, 16.0%)

Footnotes

[a]This category of serious adverse events (SAE) reports the aggregate total of possibly-, probably- and definitely-related SAEs, as attributed based on the site investigator's determination. The estimate is based on the number of related SAEs relative to the denominator of 5,000.

[b]The estimated seven-day mortality rate is based on a Kaplan-Meier estimate using all reported deaths. See methods for further estimation details including handling of censoring due to ongoing data collection.

The authors concluded that the experience from the first 5000 patients with COVID-19 transfused with convalescent plasma provides no signal of toxicity beyond what is expected from plasma use in severely ill patients. These early indicators suggest that transfusion of convalescent plasma is safe in hospitalised patients with COVID-19.[9]

Salazar E et al. (2020) conducted a case series study from March 28, 2020, to April 14, 2020 at the Houston Methodist hospitals in Texas, USA. Twenty-five patients with severe and/or life-threatening COVID-19 disease were enrolled in the study. All patients received one 300- mL dose of convalescent-phase plasma, and one patient received a second transfusion 6 days after the initial transfusion. Most patients received concomitant anti-inflammatory treatments within 5 days of the plasma transfusion, including tocilizumab and steroids. Most received other investigational treatments, including courses of hydroxychloroquine and azithromycin, ribavirin, and/or lopinavir/ritonavir; and two patients received remdesivir. Clinical outcomes and laboratory parameters were assessed at days 0, 7, and 14 after transfusion.[10]

The end point was an improvement in the modified six-point World Health Organization ordinal scale at day 14 after transfusion, including discharge from the hospital. At day 7 after transfusion, nine patients (36%) improved from baseline, 13 (52%) had no change, and three deteriorated as shown in Figure 1. Seven of the nine improved patients (28%) had been discharged. By day 14 after transfusion, 19 patients (76%) improved from baseline: an additional four patients were discharged, eight patients improved from baseline, three patients remained unchanged, three had deteriorated, and one patient died from a condition not caused by plasma transfusion (Figure 1). No adverse events attributed to plasma transfusion occurred within 24 hours after transfusion.[10]

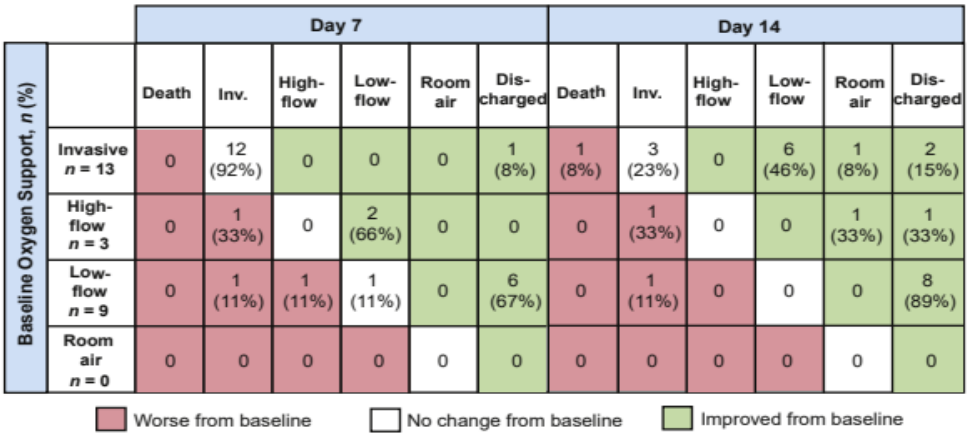

Figure 1: Clinical outcomes at days 7 and 14 after transfusion. Distribution of patients on low-flow, high-flow, invasive, or no oxygen support at days 0 (day of transfusion), 7, and 14. By day 7 after transfusion, 36% (9/25) of patients had improved from baseline; 76% (19/25) of patients improved by day 14 after transfusion. Inv., Invasive.[10]

The average overall length of hospital stay was 14.3 days (range, 2 to 25 days). The average post-transfusion length of hospital stay was 11 days (range, 1 to 21 days). No adverse events attributed to plasma transfusion occurred within 24 hours after transfusion. The authors concluded from this case series of 25 patients indicate that administration of convalescent plasma is a safe treatment option for those with severe COVID-19 disease.[10]

Zeng QL et al. (2020) conducted a case series study in The First Affiliated Hospital of Zhengzhou University and The Sixth People's Hospital of Zhengzhou City, the highest referral hospitals for COVID-19 in Henan Province, China. Twenty-one contemporaneous critically ill patients with COVID-19 were enrolled in the current study (six of the patients in the convalescent plasma treatment group and 15 patients in the control group). Death eventually occurred in 5 of 6 patients in the treatment group and 14 of 15 in the control group (P = 0.18); each group had just one recovered patient. Viral clearance was achieved after convalescent plasma transfusion in all six patients in the treatment group. Among patients who died, all five (100%) in the treatment group and three of 14 (21.4%) in the control group had undetectable SARS-CoV-2 before death (P = 0.005). The survival period was longer in the treatment group than in the control group (P = .03). No immediate or noticeable adverse effects were observed with convalescent plasma infusions.[11]

The authors concluded the study indicate that convalescent plasma treatment contributes to the discontinuation of SARS-CoV-2 shedding and longer survival in patients with COVID-19 and respiratory failure; however, it cannot reduce the mortality rate in critically ill patients with end-stage COVID-19. Hence, convalescent plasma treatment should probably be used in potentially critically ill patients COVID-19 at an early stage of disease. Thus, early recognition of patients with COVID-19 who are likely to become critically ill is key to the use of convalescent plasma treatment.[11]

Chen S et al. (2020) conducted a case series study in the First Affiliated Hospital of Zhengzhou University and Henan Provincial People's Hospital in China. Sixteen COVID-19 patients received transfusion of anti-COVID-19 antibody-positive

convalescent plasma. The main outcome was time for viral nucleic acid amplification (NAA) test turning negative. Clinical laboratory parameters were measured at the baseline (d0) before plasma transfusion, day 1 (d1) and day 3 (d3) after transfusion as well. Among the 16 patients, 10 of them had a consistently positive result of viral NAA test before convalescent plasma transfusion. Eight patients (8/10) became negative from day 2 to day 8 after transfusion. Severe patients showed a shorter time for NAA test turning negative after transfusion (mean rank 2.17 vs 5·90, P = 0.036). Two critically ill patients who were transfused plasma with lower antibody level remained a positive result of NAA test. C-reactive protein (CRP) level demonstrated a decline one day after convalescent plasma treatment, compared with the baseline (P = 0.017). No adverse events were observed during convalescent plasma transfusion.[12]

Olivares-Gazca JC et al. (2020) conducted a pilot study in three hospitals in Puebla, Mexico between April 17, 2020 and May 8, 2020 involving 10 male patients that were prospectively treated with plasma from COVID-19 convalescent donors. The patients were receiving other treatments prior to convalescent plasma: Steroids, hydroxychloroquine, azithromycin, tocilizumab and lopinazir/ritonazir. Over eight days of convalescent plasma transfusion, the sequential organ failure assessment score dropped significantly from 1736.6 to 1061.8 ng/ml (p=0.0001). Chest X-rays improved in 7/10 cases and in 6/10, computerised tomography scans also revealed improvement of the lung injury. Decreases in C-reactive protein and D-dimer levels also observed. Three of five patients on mechanical ventilation support could be extubated, nine were transferred to conventional hospital floors, and six were sent home; two patients died. The administration of convalescent plasma had no side effect and the 24-day overall survival was 77%. The authors concluded since the patients were receiving other treatments, it is difficult to conclude that the convalescent plasma infusion was fully responsible for the improvement in pulmonary function and in the patient's clinical course. However, although other treatments were also administered to the patients and as a result data are difficult to interpret, it seems that the addition of convalescent plasma improved pulmonary function.[13]

The details of patients and convalescent plasma donors are described in **Annex 1**.

CONCLUSION

Convalescent plasma therapy is a potential therapeutic option in improving clinical symptoms of the severe/critically ill patients with COVID-19. Short term data showed administration of convalescent plasma in patients with severe COVID-19 disease did not associated with severe adverse events. However, optimal dose and treatment time point, as well as the definitive statement of this therapy, need to be further investigated in randomised controlled clinical studies.

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Annex 1: Characteristics of patients and convalescent plasma donors

Study	Patients	Donors
Duan K et al (n=10)	Enrollment criteria were one of the conditions 2 to 4 plus condition 1: 1) Age ≥ 18 years 2) Respiratory distress, RR ≥30 beats/min 3) Oxygen saturation level less than 93% in resting state; and 4) Partial pressure of oxygen (PaO2)/oxygen concentration (FiO2) ≤ 300 mmHg (1 mmHg = 0.133 kPa). Exclusion criteria were as follows: 1) Previous allergic history to plasma or ingredients (sodium citrate) 2) Cases with serious general conditions, such as severe organ dysfunction, who were not suitable for CP transfusion.	10 donor patients who recovered from COVID-19 were recruited from three participating hospitals. The recovery criteria were as follows: 1) Normality of body temperature for more than 3 d, 2) Resolution of respiratory tract symptoms, and 3) Two consecutively negative results of sputum SARS-CoV-2 by RT-PCR assay (1-d sampling interval). The donor's blood was collected after 3 wk post onset of illness and 4 d post discharge. Written informed consent was obtained from each patient.
Shen C et al (n=5)	Enrollment criteria: 1) Severe pneumonia with rapid progression and continuously high viral load despite antiviral treatment; 2) PAO2/FIO2 of <300 mmHg 3) Currently or had been supported with mechanical ventilation - Age range: 36-73 years - 3 men, 2 women - None were smokers	1) Age range: 18-60 years. 2) All donors had been diagnosed with COVID-19 (laboratory confirmed) and subsequently tested negative for SARS-CoV-2 and other respiratory viruses, as well as hepatitis B virus, hepatitis C virus, HIV, and syphilis 3) Donors were asymptomatic and well for at least 10 days 4) Serum SARS-CoV-2-specific ELISA antibody titer higher than 1:1000 and a neutralizing antibody titer greater than 40

	- 4 of 5 had no pre-existing medical conditions (1 patient with hypertension and mitral insufficiency) - All patients received methylprednisolone	
Hartman W et al (n=31) (Not undergone peer review)	All enrollees had laboratory confirmed COVID-19 with either severe or life-threatening disease. Severe disease was defined as the presence of subjective 1) Dyspnea, 2) A respiratory frequency ≥ 30/min, 3) Blood oxygen saturation ≤ 93% on room air, 4) Partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, 5) And/or lung infiltrates > 50% within 24 to 48 hours. Life-threatening disease was defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure at the time of transfusion.	
Abolghasemi H et al (n=189)	Inclusion Criteria: 1) Age ≥ 18 years 2) Confirmed COVID-19 infection through laboratory (RT-qPCR) and/ or lung involvement confirmed with chest imaging (CT scan) 3) Presence of some or all of disease clinical symptoms such as shortness of breath (dyspnea), respiratory frequency ≥ 20/min, fever, and cough	Inclusion Criteria: 1) Age range: 18–60 years old. 2) Negative qRT-PCR for COVID-19 and other standard virology tests at the time of donation while their test results had been previously positive by qRT-PCR for COVID-19. 3) No remaining symptoms of COVID-19 infection at least 14 days prior to donation. 4) Tested by the semi-quantitative enzyme-linked immunosorbent assay (ELISA) antibody identification test and Rapid Strip

	4) Hospitalized with a blood oxygen saturation (SPO2) ≤93 % at rest on room air 5) ≤7 days since illness onset 6) Willingness to participate in the trail and sign the consent form Exclusion Criteria - Patients with either of following criteria excluded from the trail: 1) Intubated patients or patients on mechanical ventilation. 2) Severe liver or kidney disease 3) Septic Shock 4) Physician decision that convalescent plasma therapy is not in patients' best interest 5) Patients with improving clinical conditions who meet hospital discharge criteria (defined as clinical recovery, i.e. return of body temperature, respiratory rate, oxygen saturation to normal and cough relief). 6) Known hypersensitivity to plasma	Test (IgG 98 % Pos, IgM 75 % Pos) antibody identification test for COVID-19. 5) Donated plasmas contained antibody titer cut off index higher than 1.1 6) Perform routine screening tests for transfusion transmitted infections (HIV, HBV, HCV, RPR) Exclusion Criteria: 1) Female donors with a history of pregnancy
Joyner M et al (n=5000) (Not undergone peer review)	Of the 4,051 patients diagnosed with severe or life-threatening COVID-19, 1) 72% had respiratory failure, 2) 63% reported dyspnea, 3) 62% had a blood oxygen saturation ≤ 93%, 4) 43% had lung infiltrates >50% within 24-28 hours of enrollment, 5) 38% had a respiratory frequency ≥ 30 breaths·minute^{-1}, 6) 34% had partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, 7) 18% had multiple organ dysfunction or failure, and 8) 15% had septic shock.	
Salazar et al (n=25)	Patients were eligible if they had severe and/or life-threatening COVID19 disease.	1) Each donor had a documented history of laboratory-confirmed SARS-CoV-2 infection on the basis of a positive RT-PCR test result.

<table>
<tr>
<td></td>
<td>Severe disease was defined as one or more of the following:
1) Shortness of breath (dyspnea),
2) Respiratory rate 30/min,
3) Blood oxygen saturation 93%,
4) Partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or
5) Pulmonary infiltrates > 50% within 24 to 48 hours.

Life-threatening disease was defined as one or more of the following: respiratory failure, septic shock, and/or multiple organ dysfunction or failure.</td>
<td>2) All plasma was donated by recovered and healthy COVID-19 patients who had been asymptomatic for 14 days.
3) Age range: 23-67 years old (57% were males)
4) All donors provided written informed consent and tested negative for SARS-CoV-2 by RTPCR.
5) If eligible according to standard blood donor criteria, donors were enrolled in a frequent plasmapheresis program.
6) Donors were negative for anti-human leukocyte antigen antibodies, hepatitis B virus, hepatitis C virus, HIV, human Tlymphotropic virus I/II, Chagas disease, West Nile virus, Zika virus, and syphilis, per standard blood banking practices.</td>
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<td>Zeng QL et al

(n=21)</td>
<td>Comparison of clinical characteristics between treatment (convalescent plasma) & control (non-convalescent plasma)

<table>
<tr><th></th><th>Clinical features</th><th>Treatment group</th><th>Control group</th><th>P value</th></tr>
<tr><td>1)</td><td>fever</td><td>5(83.3)</td><td>13(86.7)</td><td>>.99</td></tr>
<tr><td>2)</td><td>cough</td><td>5(83.3)</td><td>14(93.3)</td><td>.50</td></tr>
<tr><td>3)</td><td>dyspnea</td><td>3(50)</td><td>8(53.3)</td><td>>.99</td></tr>
<tr><td>4)</td><td>Septic shock</td><td>3(50)</td><td>8)53.3)</td><td>>.99</td></tr>
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<td>1) Young adult individuals who had recovered from COVID-19 for 1–2 weeks were eligible to be considered as blood donors.
2) All donors were negative at SARS-CoV-2 RNA and immunoglobulin (Ig) M testing and positive at IgG testing before donation.
3) Seronegative for hepatitis B and C, human immunodeficiency virus, and syphilis.</td>
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