Efficacy of Convalescent Plasma to Treat Mild to Moderate COVID-19 in Kidney Transplant Patients: A Propensity Score Matching Analysis

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Kidney transplant recipients have higher mortality from coronavirus disease 2019 (COVID-19) compared with the general population.[1,2] In the absence of effective treatment,[3] the early use of convalescent plasma emerged as an alternative therapy with a favorable safety profile.

This observational, prospective, single-center, single-arm cohort study assessed the 30-d COVID-19–associated lethality in kidney transplant recipients treated with convalescent plasma. The protocol was approved by the local ethics committee, and all patients signed an informed consent form. From February 3, 2021, to March 30, 2021, nonvaccinated patients aged over 30 y with up to 10 d of real-time polymerase chain reaction–confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) mild to moderate infection based on the WHO severity criteria[4] were eligible to receive 1 single-donor ABO-compatible intravenous infusion of 200 mL of convalescent plasma. Immediately before infusion, the patients were tested for prevalence of anti-SARS-CoV-2 nucleocapsid protein (SARS-CoV-2 IgG test ARCHITECT I System, Abbott Laboratories, IL; cut off of 1.68 S/CO). Plasmas with anti-SARS-CoV-2 immunoglobulin G (IgG) ≥840 AU/mL (absorbance units per milliliter; AdviseDx SARS-CoV-2 IgG II ARCHITECT chemiluminescent immunoassay, Abbott Laboratories) or neutralizing activity ≥68% (%; cPass SARS-CoV-2 Neutralization Antibody Detection Kit, GenScript Laboratories) were labeled as "high-titer plasma" following Food and Drug Administration guidance.[5]

Between January 1, 2021, and March 30, 2021, 456 kidney transplant recipients developed real-time polymerase chain reaction–confirmed SARS-CoV-2 infection (Figure S3, SDC, http://links.lww.com/TP/C294). Of them, 58 (13%) were treated with convalescent plasma, and 116 were selected to construct the matched control group using a 1 to 2 propensity score matching (Supplementary Statistics S1, SDC, http://links.lww.com/TP/C294).

There were no differences in demographic characteristics, including comorbidities and immunosuppression (Table 1). The median time from symptoms onset to diagnosis of SARS-CoV-2 infection was 3 d in both groups, although patients in the control group had a higher proportion of patients with initial WHO severity scores between 4 and 6 (1.7% versus 6.8%; $P = 0.033$) and who received azithromycin (8.9% versus 22.2%; $P = 0.034$), respectively (Table 1).

Patients received convalescent plasma with a median time of 6 d (interquartile range [IQR], 4–7) from the first symptom. The median IgG anti-SARS-CoV-2 concentration in the plasma units was 790 AU/mL (IQR, 399–1996 AU/mL), and the median neutralization activity was 61% (IQR, 39%–85%). Only 28 (48%) were labeled as high-titer plasma units. Only 1 patient had generalized pruritus 24 h after the infusion, which was completely resolved with oral antihistamines. After 30 d from the onset of symptoms, there were no differences in the need for supplementary oxygen (Supplementary Table S1, SDC, http://links.lww.com/TP/C294) (72% versus 68%; $P = 0.684$) or mechanical ventilation (28% versus 32%; $P = 0.684$). The Cox model showed a hazard ratio for convalescent plasma of 0.94 (95% confidence interval [CI], 0.49-1.82; $P = 0.85$). All 4 (6.8%) patients with positive IgG anti-SARS-CoV-2 nucleocapsid protein immediately before infusion had a mild disease and were treated as outpatients. Compared with nonsurvivors, a trend toward a higher proportion of survivors receiving higher-titer plasma was observed based on anti-SARS-CoV-2 IgG ≥840 AU/mL (49% versus 38%; odds ratio

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TABLE 1.

Baseline characteristics, clinical presentation, and management of the 174 patients with confirmed SARS-CoV-2 infection

	Convalescent plasma (n = 58)	Matched control (n = 116)	*P*
Baseline characteristics			
Age, median (IQR)	50 (40–58)	50 (42–61)	0.676
Male gender, n (%)	39 (67)	78 (67)	>0.999
BMI >30 kg/m^2, n (%)	18 (31)	36 (31)	>0.999
Deceased donor transplants, n (%)	28 (51)	56 (50)	0.956
Prior transplant, n (%)	2 (3.6)	6 (5.4)	>0.999
Months after transplant, median (IQR)	72 (29–139)	73 (31–134)	0.926
Immunosuppression, n (%)			0.838
TAC-AZA	18 (31)	40 (35)	
TAC-MPA	19 (33)	38 (33)	
TAC-mTORi	7(12)	11 (9.6)	
Other	14 (24)	27 (22.5)	
Steroids use, n (%)	55 (98)	114 (98)	>0.999
High steroid dose within the previous 3 mo, n (%)	2 (3.9)	1 (0.9)	0.231
Antithymocyte globulin within the previous 3 mo, n (%)	2 (3.9)	1 (0.9)	0.231
Use ACE or ARB, n (%)	18 (33)	43 (39)	0.500
Current of former smoker, n (%)	9 (44)	28 (30)	0.265
Hypertension, n (%)	42 (72)	91 (78)	0.377
Diabetes, n (%)	21 (36)	39 (34)	0.735
Heart disease, n (%)	2 (3.4)	0 (0)	0.110
CKD-EPI creatinine eGFR at baseline, median (IQR)	52 (37–64)	50 (34–62)	0.725
Days from symptoms onset to COVID-19 diagnosis, median (IQR)	3 (2–4)	3 (2–5)	0.458
COVID-19 WHO severity score at presentation, n (%)			**0.033**
1—Ambulatory, asymptomatic; viral RNA detected	0	1 (0.9)	
2—Ambulatory, symptomatic; independent	46 (79.3)	62 (53.4)	
3—Ambulatory, symptomatic; assistance needed	11 (19)	45 (38.8)	
4—Hospitalized; no oxygen therapy	1 (1.7)	2 (1.7)	
5—Hospitalized; oxygen by mask or nasal prongs	0	4 (3.4)	
6—Hospitalized; oxygen by NIV or high flow	0	2 (1.7)	
Pharmacological treatment during COVID-19,[a] n (%)			
High-dose steroids	21 (37.5)	48 (44.4)	0.393
Azithromycin	5 (8.9)	24 (22.2)	**0.034**
Other antibiotics	20 (35.7)	42 (38.2)	0.756
Hydroxychloroquine	0	2 (1.7)	0.301
Ivermectin	0	2 (1.7)	0.301
Monoclonal antibodies	0	0	–
Remdesivir	0	0	–
Immunosuppression during COVID-19, n (%)			
No changes	38 (65.5)	67 (58)	0.606
Suspension of MPA/mTORi/AZA	7(12)	14(12)	
Suspension of all drugs except for steroids	13 (22.5)	28 (24)	
Missing information	0	7 (6)	
Outcomes			
Need for oxygen therapy	72%	68%	0.684
Mechanical ventilation	28%	32%	0.684
Death	22%	24%	0.950

Bold types means $P < 0.05$.

[a]One patient might have used >1 pharmacological treatment during COVID-19.

ACE, angiotensin converting enzyme; ARB, angiotensin receptor blocker; AZA, azathioprine; BMI, body mass index; CKD-EPI, chronic kidney disease epidemiology collaboration; COVID-19, coronavirus disease 2019; eGFR, estimated glomerular filtration rate; IQR, inrequartile range; MPA, mycophenolic acid; mTORi, m-TOR inhibitors; NIV, non Invasive ventilation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TAC, tacrolimus.

[OR], 0.653; 95% CI, 0.185-2.306; $P = 0.507$), neutralizing activity ≥68% (44% versus 15%; OR, 0.227; 95% CI, 0.045-1.145; $P = 0.057$), or 1 of the 2 criteria (51% versus 38%; OR, 0.598; 95% CI, 0.169-2.110; $P = 0.421$).

In summary, this prospective propensity matched cohort study showed that the use of convalescent plasma was not associated with a reduction in COVID-19 progression and lethality among kidney transplant

recipients. The small sample size, higher severity in the control group, delayed treatment, and use of a low proportion of high-titer convalescent plasma are significant confounders in this analysis. The study underscores the challenges inherent to COVID-19, including poor response to vaccination, and timely early institution of effective (high-titer plasma or monoclonal antibodies) therapy.

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