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 criteria4 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 1 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 anti-histamines. 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 = 0.83). 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...
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

**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/m², n (%)           | 18 (31)                     | 36 (31)                   | >0.999 |
| Deceased donor transplants, n (%) | 28 (61)                   | 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 (%)       |                             |                           |        |
| 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 (73)                     | 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,* 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  |

*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, interquartile range; MPA, mycophenolic acid; mTOR, m-TOR inhibitors; NIV, non invasive ventilation; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TAC, tacrolimus.

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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