The Association Between Convalescent Plasma Treatment and Survival of Patients with COVID-19

BACKGROUND

Various treatments of COVID-19 including the infusion of plasma of convalescent patients are still researched, especially for moderate and severe cases.[1–3] The published studies report conflicting efficacy of the treatment with plasma. One randomized trial showed that early administration of convalescent plasma might be effective in elderly patients[3] while another trial did not reveal the reduction in mortality.[1,2]

OBJECTIVES

The aim of this study was to investigate the association of convalescent plasma treatment and mortality among patients with COVID-19.

METHODS

This retrospective study was conducted by obtaining medical records of 9565 patients hospitalized at the Mount Sinai Health System with laboratory-confirmed COVID-19 between March 1, 2020, and March 30, 2021. Patients were stratified into groups, those treated with convalescent plasma and those not treated.

The primary outcome of interest was the in-hospital mortality. Secondary outcome was acute kidney injury, which was defined as creatinine 1.5 times or more of baseline, or $\geq$ 0.3mg/dL increase.[4] Recipients of plasma and controls were matched by propensity score using 1:1 matching scheme without replacement. Good balance was achieved for patients' baseline characteristics including age, sex, comorbidities, vital signs at admission, laboratory data, and in-hospital treatment, including therapeutic anticoagulation, steroid treatment, use of interleukin-6 inhibitor, and use of remdesivir. As a

sensitivity analysis, we analyzed the outcomes for patients with moderate or severe COVID-19, which was defined as oxygen saturation on room air $\leq$ 94% at admission. Among them, patients requiring endotracheal intubation and/or intensive care unit were defined as severe COVID-19 cases.

We performed subgroup analyses where we compared in-hospital mortality for recipients of plasma and control patients $\geq$ 75 years old (N = 3102, 32.4%), patients with steroid treatment (N = 4751, 49.7%), which is the current standard treatment,[5] and patients who were discharged between Feb 18, 2021, and March 30, 2021, to investigate the latest data.

All statistical calculations and analyses were performed in R, with p values < 0.05 were considered statistically significant.

FINDINGS

Of the 9565 patients with laboratory-confirmed COVID-19, 1113 patients (11.6%) received convalescent plasma. Baseline characteristics, other treatments, and in-hospital outcomes were not significantly different between recipients of plasma and control patients (Table 1).

After matching by propensity score (N = 960 in each group), both groups were well balanced (all standardized differences < 10%) (Table 1). In-hospital mortality and acute kidney injury were not significantly different in patients treated with and without convalescent plasma in the propensity matched cohorts (Table 1). In the analysis limiting patients to moderate or severe COVID-19 (N = 8295, 86.7%), in-hospital mortality was not significantly different in patients with and without convalescent plasma in the propensity matched cohorts (N = 930 pairs; 26.1% versus 22.4%, p = 0.066). The result was the same among severe patients (N = 278 pairs; 58.6% versus 60.8%, p = 0.67) as well as moderate patients (N = 6215 patients; 645 pairs; 10.5% versus 11.6%, p = 0.60).

Among patients $\geq$ 75 years, or patients with steroid treatment, in-hospital mortality was not different between patients with convalescent plasma and those without (Table 2). Among patients who were discharged between Feb 18, 2021, and March 30, 2021 (N = 2406), in-hospital mortality was not significantly differ-

Table 1 Baseline Characteristics and In-Hospital Outcomes of Patients Admitted with COVID-19 With and Without Convalescent Plasma Therapy

	All hospitalizations			Propensity-matched hospitalizations		
	Without convalescent plasma ($n = 8452$)	With convalescent plasma ($n = 1113$)	p value	Without convalescent plasma ($n = 960$)	With convalescent plasma ($n = 960$)	p value
Age, (mean, SD), year	65.0 (17.1)	64.8 (16.1)	0.80	64.9 (16.1)	64.5 (16.2)	0.57
Male, n (%)	4568 (54.0)	667 (59.9)	<0.001	584 (60.8)	576 (60.0)	0.74
Asthma, n (%)	499 (5.9)	44 (4.0)	0.01	42 (4.4)	40 (4.2)	0.91
COPD, n (%)	369 (4.4)	57 (5.1)	0.28	49 (5.1)	46 (4.8)	0.83
Hypertension, n (%)	3094 (36.6)	381 (34.2)	0.13	329 (34.3)	337 (35.1)	0.74
Diabetes mellitus, n (%)	2017 (23.9)	228 (20.5)	0.014	191 (19.9)	200 (20.8)	0.65
Chronic kidney disease, n (%)	1017 (12.0)	127 (11.4)	0.58	114 (11.9)	115 (12.0)	1.00
Cancer, n (%)	734 (8.7)	130 (11.7)	0.001	107 (11.1)	110 (11.5)	0.89
Heart failure, n (%)	777 (9.2)	83 (7.5)	0.065	75 (7.8)	67 (7.0)	0.54
Oxygen saturation, (median [IQR])	90.0 [84.0, 93.0]	88.0 [79.0, 91.0]	<0.001	88.0 [79.0, 91.0]	88.0 [79.8, 91.0]	0.74
Respiratory rate, (median [IQR])	19.0 [18.0, 21.0]	20.0 [18.0, 22.0]	<0.001	20.0 [18.0, 23.0]	20.0 [18.0, 22.0]	0.26
D-dimer, μg/mL (median [IQR])	1.42 [0.78, 2.70]	1.06 [0.64, 1.94]	<0.001	1.21 [0.70, 2.02]	1.06 [0.64, 1.90]	0.004
C reactive protein, mg/L (median [IQR])	88.1 [37.1, 167.1]	85.8 [43.9, 161.6]	0.47	92.5 [45.7, 157.1]	84.3 [42.7, 159.6]	0.50
Therapeutic anticoagulation during hospitalization, n (%)	2604 (30.8)	525 (47.2)	<0.001	436 (45.4)	426 (44.4)	0.68
Steroid during hospitalization, n (%)	3802 (45.0)	949 (85.3)	<0.001	810 (84.4)	817 (85.1)	0.70
Use of remdesivir	1066 (12.6)	530 (47.6)	<0.001	438 (45.6)	448 (46.7)	0.68
Use of IL-6 inhibitor	274 (3.2)	50 (4.5)	0.038	45 (4.7)	42 (4.4)	0.83
ICU admission	1592 (18.8)	332 (29.8)	<0.001	282 (29.4)	270 (28.1)	0.58
Endotracheal intubation, n (%)	1052 (12.4)	214 (19.2)	<0.001	182 (19.0)	177 (18.4)	0.82
In-hospital death, n (%)	1961 (23.2)	279 (25.1)	0.18	250 (26.0)	241 (25.1)	0.68
Acute kidney injury, n (%)	2313 (27.8)	319 (28.7)	0.56	273 (28.4)	261 (27.2)	0.58

COPD chronic obstructive pulmonary disease, ICU intensive care unit, IL-6 interleukin-6, SD standard deviation

ent in patients with and without convalescent plasma treatment in the propensity-matched cohorts (171 pairs; 25.7% versus 19.3%, $p = 0.20$).

DISCUSSION

Convalescent plasma was expected to be effective for treatment of COVID-19 patients; however, the most recent randomized trial did not demonstrate the benefit of mortality reduction.[6] Our study supports no reduction in mortality with convalescent plasma treatment among COVID-19 patients including subgroup analyses of patients age ≥ 75 years old, on steroid treatments, among moderate to severe, and severe patients.

Our study is not without limitations. First, this is an observational study in which we could not fully adjust for unobserved confounders. Second, we do not have information of the titer and timing of convalescent plasma, which might affect our results.[6] Finally, we do not have the admission date, which might affect the decision whether to use convalescent plasma.

In conclusion, convalescent plasma treatment was not associated with a lower risk of in-hospital mortality of COVID-19 patients. Further investigation is required to confirm these findings.

Table 2 Baseline Characteristics and In-Hospital Outcomes of Patients Above 75, or Patients with Steroid Treatments Admitted with COVID-19 With and Without Convalescent Plasma Therapy

	All hospitalizations			Propensity-matched hospitalizations		
Patients above 75 years old	**Without convalescent plasma (*n* = 2766)**	**With convalescent plasma (*n* = 336)**	***p* value**	**Without convalescent plasma (*n* = 274)**	**With convalescent plasma (*n* = 274)**	***p* value**
Age, (mean, SD), year	83.0 (5.0)	82.6 (5.1)	0.20	83.1 (4.8)	82.8 (5.1)	0.44
Male, *n* (%)	1274 (46.1)	176 (52.4)	0.033	142 (51.8)	141 (51.5)	1.00
Hypertension, *n* (%)	1271 (46.0)	153 (45.5)	0.93	127 (46.4)	128 (46.7)	1.00
Diabetes mellitus, *n* (%)	681 (24.6)	69 (20.5)	0.11	61 (22.3)	61 (22.3)	1.00
Heart failure, *n* (%)	368 (13.3)	39 (11.6)	0.43	32 (11.7)	32 (11.7)	1.00
Oxygen saturation, (median [IQR])	90.0 [80.0, 92.0]	86.0 [73.8, 90.0]	<0.001	86.0 [76.0, 90.0]	86.5 [76.3, 90.0]	0.66
Therapeutic anticoagulation during hospitalization, *n* (%)	1056 (38.2)	186 (55.4)	<0.001	138 (50.4)	149 (54.4)	0.39
Steroid during hospitalization, *n* (%)	1302 (47.1)	296 (88.1)	<0.001	242 (88.3)	241 (88.0)	1.00
ICU admission	465 (16.8)	97 (28.9)	<0.001	69 (25.2)	75 (27.4)	0.63
Endotracheal intubation, *n* (%)	334 (12.1)	66 (19.6)	<0.001	48 (17.5)	49 (17.9)	1.00
In-hospital death, *n* (%)	1054 (38.1)	132 (39.3)	0.72	124 (45.3)	108 (39.4)	0.20
Acute kidney injury, *n* (%)	933 (33.9)	118 (35.1)	0.69	98 (35.8)	92 (33.6)	0.65
Patients with steroid treatments	**Without convalescent plasma (*n* = 3802)**	**With convalescent plasma (*n* = 949)**	***p* value**	**Without convalescent plasma (*n* = 816)**	**With convalescent plasma (*n* = 816)**	***p* value**
Age, (mean, SD), year	66.8 (15.4)	65.2 (16.1)	0.005	64.9 (15.6)	64.8 (16.1)	0.97
Male, *n* (%)	2106 (55.4)	573 (60.4)	0.006	486 (59.6)	489 (59.9)	0.92
Hypertension, *n* (%)	1419 (37.3)	324 (34.1)	0.075	276 (33.8)	283 (34.7)	0.75
Diabetes mellitus, *n* (%)	921 (24.2)	186 (19.6)	0.003	158 (19.4)	166 (20.3)	0.66
Heart failure, *n* (%)	341 (9.0)	67 (7.1)	0.07	54 (6.6)	56 (6.9)	0.92
Oxygen saturation, (median [IQR])	78.0 [63.0, 87.0]	73.0 [50.0, 84.0]	<0.001	72.0 [46.3, 85.0]	73.0 [51.3, 83.8]	0.79
Therapeutic anticoagulation during hospitalization, *n* (%)	1438 (37.8)	438 (46.2)	<0.001	333 (40.8)	354 (43.4)	0.32
ICU admission	1072 (28.2)	314 (33.1)	0.003	260 (31.9)	259 (31.7)	1.00
Endotracheal intubation, *n* (%)	718 (18.9)	203 (21.4)	0.089	170 (20.8)	167 (20.5)	0.90
In-hospital death, *n* (%)	1050 (27.6)	250 (26.3)	0.46	205 (25.1)	217 (26.6)	0.53
Acute kidney injury, *n* (%)	1182 (31.1)	280 (29.5)	0.35	226 (27.7)	231 (28.3)	0.83

ICU intensive care unit, SD standard deviation

Toshiki Kuno, MD, PhD[1]
Mai Takahashi, MD, MPH[1]
Natalia N. Egorova, PhD, MPH[2]

[1]Department of Medicine, Icahn School of Medicine at Mount Sinai, Mount Sinai Beth Israel,
New York, NY, USA
[2]Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai,
New York, NY, USA

Corresponding Author: *Toshiki Kuno, MD, PhD; Department of Medicine, Icahn School of Medicine at Mount Sinai, Mount Sinai Beth Israel, New York, NY, USA (e-mail: toshiki.kuno@mountsinai.org).*

Declarations:

This study was approved by the institutional review boards (#2000495) and conducted in accordance with the principles of the Declaration of Helsinki. The waiver of patients' informed consent was also approved by the institutional review boards.

Conflict of Interest: *The authors declare that they do not have a conflict of interest.*

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