

Bed-sided short-duration renal replacement therapy provide a possible option to treat non-critical coronavirus disease 2019 in maintenance hemodialysis patients in public health crisis

Yanglin Hu¹  | Can Tu^{1,2} | Jun-Wu Dong³ | Wen-Li Chen⁴ |
Xiao-Hui Wang⁵ | Dan Luo⁶ | Ming Shi⁷ | Mengliang Zhou⁸ | Yuting Song⁸ |
Chun Zhang⁹ | Fei Xiong¹

¹Department of Nephrology, Wuhan No. 1 Hospital, Wuhan, China

²The Second Affiliated College of Medicine, Guangzhou University of Chinese Medicine, Guangzhou, China

³Wuhan Fourth Hospital, Puai Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

⁴The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

⁵Department of Nephrology, Wuhan No. 5 Hospital, Wuhan, China

⁶Department of Nephrology, Wuhan Third Hospital (Tongren Hospital of Wuhan University), Wuhan, China

⁷Department of Nephrology, Renmin Hospital of Wuhan University, Wuhan, China

⁸The First Affiliated Medical College, Hubei University of Traditional Chinese Medicine, Wuhan, China

⁹Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Correspondence

Fei Xiong M.D Ph.D, Professor and chief,
Department of Nephrology, Wuhan
No. 1 Hospital, Zhongshan Road, 215#
Qiaokou Area, Wuhan, Hubei 430022,
China.
Email: xiongf23@sina.com

Chun Zhang M.D Ph.D, Professor and
Chair, Department of Nephrology, Union
hospital, Tongji Medical College,
Huazhong University of Science and
Technology, 1277 Jie Fang Avenue,
Wuhan, Hubei, 430022, China.
Email: drzhangchun@hust.edu.cn

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Abstract

HD care may experience great stress with the coronavirus disease 2019 (COVID-19) pandemic. A modified HD modality named bed-sided short-duration renal replacement therapy (BSRRT) was used in noncritical maintenance HD (MHD) patients diagnosed with COVID-19 in Wuhan due to extreme situation. To determine the safety and efficacy as a substitution for intermittent HD (IHD), we conducted this study. We used the data of 88 non-critical COVID-19 MHD patients collected from 65 medical units at the hospitals in Wuhan, China, from January 1 to March 10, 2020. *t*-test, Wilcoxon rank sum test, and Fisher exact probability method were used to compare the baseline characteristics, treatment, and death. Log-rank test and Cox regression multivariate analysis was used to compare the survival of noncritical patients who were transferred to BSRRT modality versus those who were continued on the IHD. Univariate analysis showed the level of reported fatigue symptom at present, bilateral lung computed tomography infiltration and steroid treatment differed between the two groups. The outcome of death of the two groups did not show significant differences in univariate analysis ($P = .0563$). Multivariate Cox regression analysis dialysis showed modality of treatment after COVID-19 diagnosis was not a significant predictor of death ($P = .1000$). These data

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suggest that for noncritical COVID-19 MHD patients, the transfer from IHD to BSRRT does not have significant difference in the risk of death compared with IHD group. This finding suggests this modified modality could be an option for the substitution for IHD during the COVID-19 pandemic period.

KEYWORDS

coronavirus disease 2019, hemodialysis patient, intervention, public crisis

1 | INTRODUCTION

The care for the large number of kidney dialysis patients who routinely undergo treatment 2-3 times per week in hospital during coronavirus disease 2019 (COVID-19) outbreak is posing an especially difficult problem for physicians.¹⁻⁴ The vulnerable ESRD patients on maintenance HD (MHD) who have already had a life-threatening disease, the high risk of exposure to coronavirus with dozens of people receiving treatment together in one room, the impending threat of coronavirus spread in facilities, the shortage of medical care personnel, and under-equipped hospitals are some of the reasons why MHD patients need particular attention.¹⁻⁴

Wuhan, as the first and one of the most severe COVID-19 epicenters, had 7154 patients receiving MHD in 65 different hospitals during the time of the COVID-19 outbreak.⁵ In our fight against the coronavirus outbreak, managing MHD patients, particularly isolating the COVID-19 MHD patients from others who were not infected, posed a big challenge.

Many HD modalities are now used including the routine intermittent HD (IHD) modalities such as HD and hemodiafiltration (HDF), and also other HD modalities such as continuous renal replacement therapy (CRRT), sustained low-efficiency dialysis, and prolonged intermittent renal replacement therapy.⁶

But in the setting of COVID-19 outbreak, with the shortage of HD machines, the potential progression of the disease, the need to quarantine, and treatment of the diagnosed COVID-19 patients,¹⁻⁴ an adapted HD modality was used in Wuhan. This was characterized by high therapy-dose (>35 mL/kg/h), low-blood flow (180-200 mL/min) and bed-sided short-duration (4-6 hours) renal replacement therapy (BSRRT). We used BSRRT as a specialized therapy used in the time of public health emergency. We report our technical and clinical experience with BSRRT as an alternative to the traditional models, and also retrospectively compared BSRRT with conventional IHD treatment on noncritical COVID-19 MHD patients. Our aim is to find an efficient use of medical resources to make the right call and save more lives with the best strategy of treatment.

2 | PATIENTS AND METHODS

2.1 | Study design, setting, and population

Once a MHD patient was diagnosed with COVID-19, the nephrologists evaluated the severity of the disease as mild, moderate, severe, or critical according to the diagnostic criteria (see below). The patients would be isolated. The noncritical patients (mild and moderate) would be put in BSRRT or IHD according to individual nephrologist's decision. It was mainly decided according to the need for isolation, the medical resources, and the patients' situation.

We collected all the clinical data of noncritical COVID-19 patients treated with BSRRT and compared the baseline characteristics, clinical characteristics, laboratory results, treatment, and outcomes with those treated with IHD. Symptoms were the collected as the first symptom since onset. Other clinical data including blood sample, BP, SPO₂, and CT were collected as the day the diagnosed patients were admitted. The average baseline day of BSRRT group was 3.2135 ± 2.2948 (mean \pm SD) days. The average baseline day of IHD group was 5.74 ± 4.62 (mean \pm SD) days.

It is a multicenter retrospective and observational study of noncritical COVID-19 MHD patients in 65 HD units in Wuhan China from January 1 and March 10, 2020. The data were collected from the online registration system of the Wuhan Hemodialysis Quality Control Center (WHQCC). And the data were further completed by contact with the patient's family members, by the medical personnel who were in charge of the patients. The baseline data cutoff for the study was March 10, 2020. The outcome of the patients was updated later on till May 8.

2.2 | Diagnostic criteria

We defined noncritical COVID-19 patients as those who fit the diagnostic criteria of mild and moderate COVID-19 patients according to New Coronavirus Pneumonia

Prevention and Control Program (seventh edition) published by the National Health Commission of China.⁵ Mild cases indicate patients have mild clinical symptoms; moderate cases indicate patients have symptoms such as fever and respiratory tract symptoms, and with abnormalities in CT scan. Severe cases indicating adults who meet any of the following criteria: (a) respiratory rate >30 breaths/min; (b) oxygen saturations <93% at a rest state; (c) arterial partial pressure of oxygen (PaO₂)/oxygen concentration (FiO₂) <300 mm Hg. Patients with >50% lesions progression within 24 to 48 hours in lung imaging. Critical cases indicating patients meeting any of the following criteria: (a) occurrence of respiratory failure requiring mechanical ventilation; (b) presence of shock; and (c) other organ failure. In addition to that, we excluded the patients who gave up therapy, whose BP were less than 90/60 mm Hg, who

did BSRRT as a transient therapy (defined by less than a week), who initially had a myocardial infarction and those with unattainable HD information after COVID-19 diagnosis (shown in Figure 1). And it should be noted that the diagnosis of COVID-19 was based on the positivity of the quantitative real-time reverse transcription-polymerase chain reaction (RT-PCR) test for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) RNA from throat swab specimens, but not by SARS-CoV-2 serum-specific antibody. Because the SARS-CoV-2 serum-specific antibody test was not widely used before March 10, 2020, and had a proportion of false positives, only patients with infection confirmed by quantitative real-time RT-PCR were included in this study. The swab was done multiple times decided by the nephrologists, all the patient had at least one positive SWAP result.

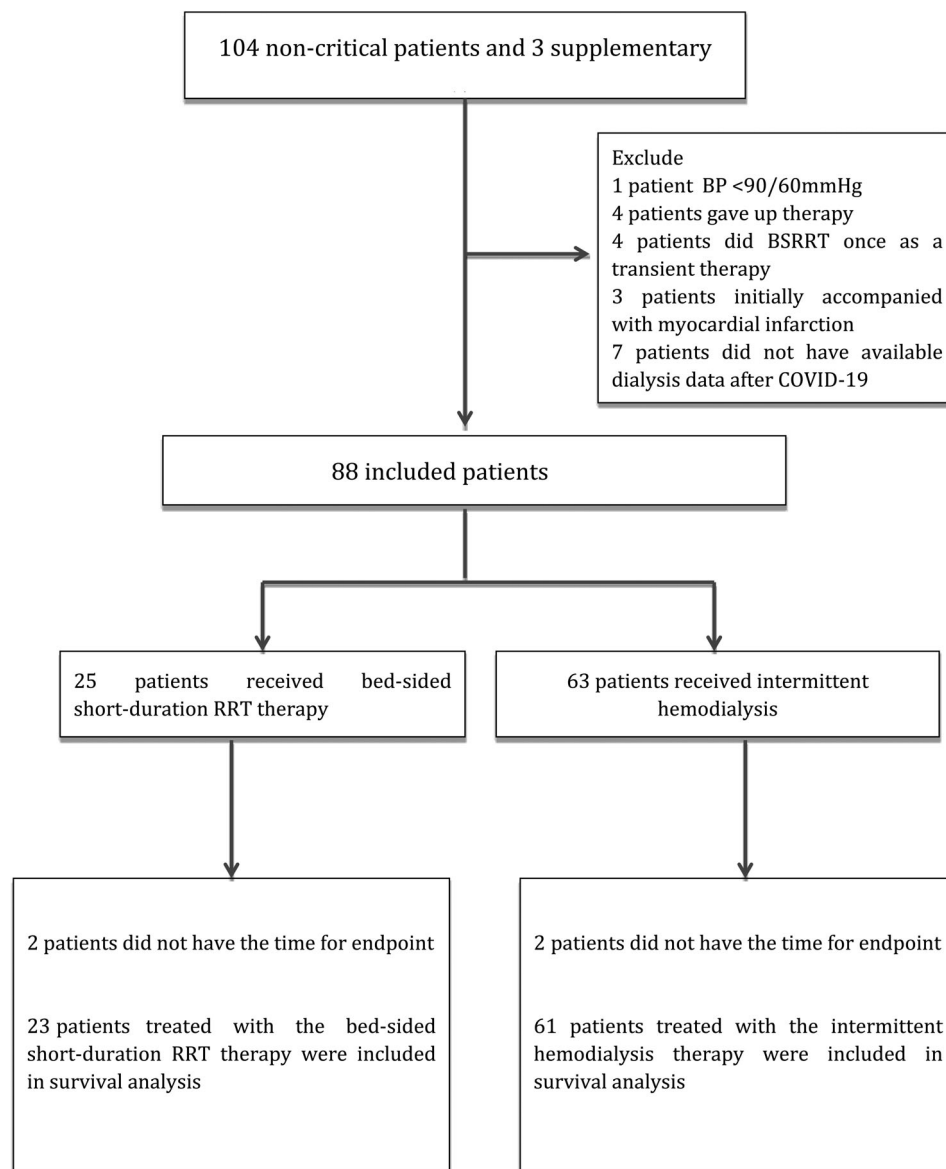


FIGURE 1 Patient disposition

2.3 | Mode of RRT

Routine HD was performed by HD center specialized nurses in center. BSRRT was also performed by HD center specialized nurses but was performed in an isolated space such as a temporary room treated for a single patient in the hospital or designated dialysis center especially for COVID-19 patients, or at the emergency specialty field hospital Leishenshan and Huoshenshan. The machines used for CRRT could all be used for BSRRT. Nurse shifts were typically 4-6 hours according to the prescription and one shift was enough. But they needed to monitor machines and record details of the treatment as with CRRT.

Routine HD modality for MHD patients is IHD consisting of HD and HDF defined as blood flow of 200-250 mL/min, treatment duration of 4 hours, treatment frequency 2-3 times/week, dialysate flow rate 500 mL/min and without or with substitution fluid flow 10-40 L/session (pre-dilution or post-dilution). BSRRT modality is characterized as low blood flow of 180-200 mL/min, high treatment therapy dose (>35 mL/kg/h), and treatment duration of 4-6 hours, 2-4 times per week depending on patient needs. The treatment therapy dose needs to be at least 35 mL/kg/h, with an average of 70 mL/kg/h. Anti-coagulation was routinely prescribed similarly to CRRT by giving loading dose and maintenance dose according to the body weight. Clinical abnormalities and electrolytes test were closely monitored.

2.4 | Endpoints and covariates

The endpoint was all-cause death. The covariates considered for Cox regression included baseline time, age, BMI, systolic BP, diastolic BP, whether the patient had diabetes, whether the patient had cardiovascular disease, the ultrafiltration volume, the dialysis modality before COVID-19, dialysis time before COVID-19, symptom of fatigue, symptom of fever, symptom of dyspnea, Hb, albumin, CT presentation, treatment with steroids, treatment with antibiotics, treatment with traditional Chinese drugs, and complications during the treatment.

2.5 | Statistical analysis

Quantitative variables were expressed as mean (SD), or median (interquartile range) depending on whether they fitted the normal distribution and the comparisons between two groups (IHD and BSRRT) were performed using *t*-test or Wilcoxon rank sum test. For qualitative variables, statistical description was expressed as

frequency (percentage), and Fisher exact probability method was chosen for comparisons between two groups. The log-rank test was used to compare the survival curves of the two groups. The potential covariates were chosen by the comparisons between two groups or the professional background. Due to the limit of the final sample size, only one covariate and the group variable were included in each multivariable Cox model to explore the adjusted effect of HD modality on the death endpoint. Statistical software was R version 3.6.3 (The R Foundation), and all hypothesis tests were two-sided tests with a significance level of .05.

3 | RESULTS

3.1 | Patient baseline characteristics

Eighty-eight patients fulfilled inclusion criteria and were enrolled into our study. Among them, 25 (28.4%) patients were switched to BSRRT and 63 (71.6%) patients stayed the routine IHD after the diagnosis of COVID-19. Baseline general and clinical characteristics, laboratory results, dialysis characteristics before COVID-19, treatment, death, and complications during therapy of two group patients were shown in Tables 1-4. Baseline general characteristics of IHD group and BSRRT group had no statistic differences (Table 1). But in baseline clinical characteristics, more patients in BSRRT group had the feeling of fatigue compared to patients in IHD group with statistical significance (62.5% vs 36.51% $P = .0331$). And CT scan showed more lateral abnormalities in BSRRT group compared to IHD group with statistical significance (96% vs 76.47%, $P = .04696$). Also more patients were treated with steroids in BSRRT group compared to IHD group patients with statistical significance (25% vs 5.45%, $P = .0199$). The complications during treatment did not have significant differences ($P > .05$).

3.2 | BSRRT prescriptions

The prescription of the 25 patients who received BSRRT therapy was shown in Table 5. The duration was 4-6 hours with most of them were 4 hours per episode with the frequency of 2-4 times per week. The therapy dosages were all high dose which was more than 35 mL/kg/h, with an average of 70 mL/kg/h. The dialyzer membrane was mainly polysulfone membrane and the blood flow during the therapy was 180-200 mL/min. During the dialysis treatment, two of them had cramp, one of them had mild hyperglycemia after treatment (5.8 mg/dL), one

TABLE 1 Baseline general characteristics of noncritical COVID-19 maintenance hemodialysis patients according to the dialysis modality after infection

	IHD (N = 63)	BSRRT (N = 25)	P-value
Age (years), mean (SD)	63.11 (13.76)	59.04 (12.96)	.2066
Gender male, n (%)	29 (46.03)	12 (48.00)	1.0000
Gender female, n (%)	34 (53.97)	13 (52.00)	1.0000
BMI (kg/m ²), mean (SD)	22.32 (4.31)	22.52 (3.70)	.8343
Systolic BP (mm Hg), mean (SD)	147.39 (18.93)	146.14 (20.26)	.8099
Diastolic BP (mm Hg), mean (SD)	85.29 (12.52)	83.05 (13.69)	.5246
SPO ₂ (%), mean (SD)	96.79 (5.25)	96.71 (2.02)	.9627
History of smoking, n (%)	16 (25.40)	6 (24.00)	1.0000
Contact with COVID-19 patients, n (%)	31 (49.21)	10 (45.45)	.8083
COVID-19 patients in the family, n (%)	15 (23.81)	4 (18.18)	.7686
Primary disease of ESRD, n (%)			
Glomerulonephritis	11 (17.46)	6 (24.00)	.5528
Polycystic kidney	2 (3.17)	0 (0.00)	1.0000
Lupus	2 (3.17)	1 (4.00)	1.0000
Other	18 (28.57)	3 (12.00)	.1641
Comorbidity of ESRD, n (%)			
Diabetes	13 (20.63)	6 (24.00)	.7771
Hypertension	10 (15.87)	8 (32.00)	.1406
Cardiovascular disease	41 (65.08)	15 (60.00)	.8063
Cerebrovascular disease	0 (0.00)	1 (4.00)	.2841
Other	22 (34.92)	7 (28.00)	.6203
Medication history, n (%)			
ACEI/ARB	18 (28.57)	8 (36.36)	.5926
Immunosuppressive drugs	3 (4.76)	3 (13.64)	.1765

Abbreviations: ACEI/ARB, angiotensin-converting enzyme inhibitors /angiotensin receptor blockers; BSRRT, bed-sided short-duration renal replacement therapy; IHD, intermittent hemodialysis.

had acute coronary syndrome. But all of them recovered after treatment.

The indications, the dosage, and the treatment time were based on the choice of individual nephrologists. The variability in the treatment dosage in the BSRRT group was based on the individual nephrologist's decisions. Each nephrologists designed the treatment dosage according to the patient's clinical severity and medical resources.

3.3 | Prognosis analysis

Survival time analysis showed the overall 60 days survival rate was 64.47% and 80 days survival rate was 42.98%. Thirty days survival rate of IHD group was 82.1% and 30 days survival rate of BSRRT was 67.0%; and 60 days survival rate of IHD group was 61.5% and 60 days survival rate of BSRRT was 54.7%. To compare the survival time, log-rank test was used. The result of

which was negative, this conclude that there was no significant difference of survival rate between two groups ($P = .1000$) (shown in Figure 2). The median survival time of BSRRT group is 65 days (shown in Figure 2). Multivariate Cox regression analysis also showed the HD modality was not a risk factor of death. However, heart injury during treatment hazard ration (HR) 6.747; 95% confidence interval (CI), 2.3006–19.785; $P = .000506$, liver injury during treatment (HR 3.969; 95% CI, 1.33–11.77; $P = .0129$), and steroid treatment (HR 3.424; 95% CI, 1.1795–9.94; $P = .0236$) were found to be risk factors for death in the multivariate Cox regression analysis (data not shown). Acute cardiac injury were diagnosed if the serum levels of cardiac biomarkers (eg, troponin I) were above the 99th percentile upper reference limit or new abnormalities were shown in electrocardiography and echocardiography. Acute hepatic injury was defined as an elevation in aspartate aminotransferase or alanine aminotransferase of >2 times the upper limit of normal.

TABLE 2 Baseline characteristics of symptoms and laboratory results of noncritical COVID-19 maintenance hemodialysis patients according to the dialysis modality after infection

	IHD (N = 63)	BSRRT (N = 25)	P-value
Symptom, n (%)			
Fever	28 (44.44)	16 (64.00)	.1554
Fatigue	23 (36.51)	15 (62.50)	.0331
Pharyngalgia	4 (6.56)	2 (8.33)	1.0000
Dry cough	20 (32.26)	7 (29.17)	1.0000
Sputum	11 (17.74)	10 (40.00)	.0501
Vomiting	8 (12.90)	3 (12.50)	1.0000
Diarrhea	7 (11.29)	3 (12.50)	1.0000
Dyspnea	11 (18.03)	6 (24.00)	.5588
Laboratory results, median (IQR)			
Hemoglobin (g/L)	109 (89, 116)	96.5 (80.62, 105)	.0949
Lymphocyte (10 ⁹ /L)	0.81 (0.46, 0.99)	0.81 (0.5, 1.24)	.8188
Albumin (g/L)	36.7 (33.78, 39.35)	39.4 (32.77, 41.17)	.2768
ALT (U/L)	9.15 (7.25, 12.5)	12.5 (8.75, 18.5)	.2651
AST (U/L)	12.75 (9.75, 17.12)	15 (10.85, 22.5)	.5932
Troponin I (μg/L)	0.08 (0.02, 0.11)	0.02 (0.01, 0.06)	.3676
TB (μmol/L)	6.65 (4.55, 7.28)	8.4 (4.35, 11)	.3527
CK (U/L)	55 (42, 82)	82 (33.75, 121.25)	.3796
CKMB (U/L)	13 (10, 15.1)	18.5 (1.6, 28.2)	.8562
LDH (U/L)	257.5(162.88, 328.88)	234 (187, 255)	.6769
iPTH (pg/mL)	262.65 (227.85, 449.25)	350.7 (51.68, 703.38)	1.0000
D dimer(mg/L)	0.9 (0.49, 1.82)	2 (1.66, 4.46)	.0569
CT manifestation, n (%)			
Ground-glass/patchy opacity	44 (86.27)	22 (88.00)	1.0000
Cord shadow	2 (3.92)	2 (8.00)	.5942
Consolidation	1 (1.96)	0 (0.00)	1.0000
Other	4 (7.84)	1 (4.00)	1.0000
Bilateral	39 (76.47)	24 (96.00)	.0496
Right	5 (9.80)	1 (4.00)	.6571
Left	5 (9.80)	0 (0.00)	.1649

Abbreviations: BSRRT, bed-sided short-duration renal replacement therapy; CKMB, creatine kinase MB isoenzyme; IHD, intermittent hemodialysis; IQR, interquartile range; LDH, lactate dehydrogenase; TB, tuberculosis.

4 | DISCUSSION

The human-to-human transmission ability of COVID-19,⁷ the altered immune function of MHD patient,^{8,9} the impossibility of quarantining MHD patients at home, the shortage of the supply of the protective equipment for all the patients and medical personnel, the shortage of the CRRT machines, and the large amount of patients infected challenged all dialysis centers in Wuhan at the very beginning of the outbreak of COVID-19.

We designed the BSRRT to isolate and treat the suspected or diagnosed noncritical COVID-19 MHD patients before the setup of a COVID-19-designated dialysis hospital.¹⁰ We also used this HD modality in some patients isolated at the field hospital later on. We felt that for the bed-sided individual HD therapy of the noncritical COVID-19 patients, the machine used for CRRT was our only choice but it might not be necessary to extend treatment time to 24 hours. To compensate the relatively low efficiency per hour and short duration, we increased

FIGURE 2 Kaplan Meier estimation of survival rates in the two groups by renal replacement modality after diagnosis of COVID-19 [Color figure can be viewed at wileyonlinelibrary.com]

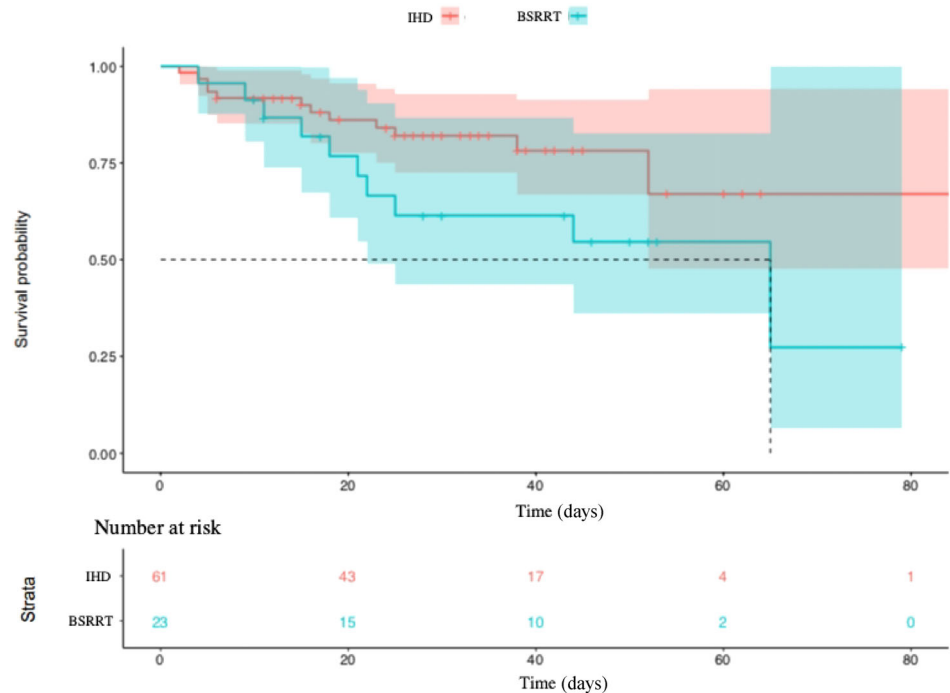


TABLE 3 Baseline dialysis characteristics and treatment of noncritical COVID-19 maintenance hemodialysis patients according to the dialysis modality after infection

	IHD (N = 63)	BSRRT (N = 25)	P-value
Dialysis before COVID-19			
Hemodialysis modality, n (%)			
Hemodialysis	22 (34.92)	10(43.48)	.6148
Hemodiafiltration	17 (26.98)	7(30.43)	.7894
Ultrafiltration volume (L), mean (SD)	2.2 (0.97)	2 (0.87)	.4149
Dialysis frequency (times/week), median (IQR)	3 (2.5, 3)	3 (3, 3)	.5306
Dialysis year (years), median (IQR)	2.46 (0.8, 5.84)	3.25 (0.63, 6.99)	.6664
Treatment, n (%)			
Antivirals	44 (77.19)	19 (79.17)	1.0000
Antibiotics	42 (77.78)	18 (78.26)	1.0000
Steroids	3 (5.45)	6 (25.00)	.0199
Traditional Chinese medicine	38 (60.32)	15 (60.00)	1.0000
Noninvasive ventilation	11 (20.00)	4 (16.67)	1.0000

Abbreviations: BSRRT, bed-sided short-duration renal replacement therapy; IHD, intermittent hemodialysis; IQR, interquartile range.

TABLE 4 Death and complications during treatment of noncritical COVID-19 maintenance hemodialysis patients according to the dialysis modality after infection

	IHD (N = 63)	BSRRT (N = 25)	P-value
Death, n (%)	12 (19.05)	10 (40.00)	.0563
Complication during treatment, n (%)			
Heart injury	7 (17.95)	5 (25.00)	.5179
Liver injury	5 (11.36)	3 (14.29)	.7063

Abbreviations: BSRRT, bed-sided short-duration renal replacement therapy; IHD, intermittent hemodialysis.

TABLE 5 Specific bed-sided short-duration RRT therapy prescription

No	Time- duration (h)	Dialysis dosage (mL/kg/h)	Dialysis machine	Dialysis membrane	Anti- coagulation drugs	Blood flow mL/min	Dialysate flow speed (L/H)	Replacement flow speed (L/H)	Ultrafiltration volume (L)	Complications	Dialysis frequency/ week
1	4	>35	1	1	NA	150	NA	NA	NA	0	2
2	4	>35	1	Asahi Kasei 18u	1	150-200	NA	0	3	0	2.5
3	4	37	4	NA	1	200	2	0	3	Cramps	2
4	4	34	4	NA	1	180	2	0	3	Cramps	2.5
5	4	77.6	3 and 2	2 and 1	1	200	3	1	0.7	0	3
6	4	78	3 and 2	2 and 1	1	200	3	1	2	0	3
7	4-6	>35	2	NA	1	150-200	NA	NA	NA	0	2
8	4	81	2	Polysulfone	1	180	2	2	2.6	0	2
9	4-6	>35	NA	NA	NA	150-200	NA	NA	NA	0	3
10	6	47.7	2	EC-1A20	1	200	1	3	1.2	0	3
11	4	63.9	2	1	1	200	2	2	2.5	0	3
12	4	>35	1	NA	1	150-200	NA	NA	NA	0	2
13	4	57.5	2	1	1	180	1.5	1.5	2.5	0	3.5
14	4-6	>35	2	NA	1	150-200	NA	NA	NA	0	2.5
15	4	96	2	Polysulfone	1	200	2	2	2.8	Mild hyper potassium	2.5
16	4-6	>35	3	NA	1	150-200	NA	NA	NA	0	3
17	4	62.2	3 and 2	2 and 1	1	200	3	1	0.5	0	2
18	4	66	3 and 2	2 and 1	1	200	3	1	3.6	0	3.5
19	4	68.4	3 and 2	2 and 1	1	200	3	1	1.5	0	3
20	4	76.8	3 and 2	2 and 1	1	200	3	1	2.3	0	2
21	4	75.3	3 and 2	2 and 1	1	200	3	1	3.6	0	4
22	4	72.7	3 and 2	2 and 1	1	200	3	1	2.9	0	3
23	4	55.5	2	1	1	180	2.5	1.5	2.5	Heart ischemia	3
24	4	78.3	2	1	1	200	4	0	2.8	0	2
25	4	71.9	3 and 2	2 and 1	1	200	3	1	2.7	0	3

Notes: Dialysis Machine: 1: B Braun Medical; 2: Fresenius Multifiltrate; 3: Asahi Kasei. Dialyzer: 1: AV600S; 2: ABH-15F; Anticoagulation drug: 1: Low molecular heparin.

therapy dose of the treatment. Although it is still controversial whether increasing the therapy dose can improve the survival of acute kidney injury patients, still we believe that when it comes to MHD patients increasing the therapy dose can increase the dialysis efficiency.^{11–13} And in fact, the actual therapy dose patients received was relatively less than the dose prescribed. But each attending nephrologist who was in charge of the patients prescribed the specific therapy dose that may vary from person to person. So in general, BSRRT modality is characterized as low blood flow of 180–200 mL/min, high treatment therapy dose (>35 mL/kg/h), and treatment duration 4–6 hours, 2–4 times per week depending on patient needs. The treatment therapy dose needs to be at least 35 mL/kg/h, with an average of 70 mL/kg/h. Anticoagulation was routinely prescribed like CRRT giving a loading dose and a maintenance dose according to the body weight (Table 5). In comparison to 24 h of CRRT, each treatment gave patients 18–20 additional non-RRT hours, thus increasing the patients' quality of life, decreasing the contact time between nurses and patients, and also increasing the success rate of complete the therapy, decreasing the clotting of the extracorporeal circuit.

As it was hard to measure the adequacy of BSRRT, as our study retrospectively compared BSRRT- and IHD-treated diagnosed noncritical COVID-19 MHD patients. We were hoping we could have some conclusion of this modified HD modality in the public health crisis and know more about COVID-19 in MHD patients.

The data showed that the overall mortality rate in 60 days was 35.53%. We can speculate that the mortality rate should be higher than ordinary COVID-19 patients, which is around 2.3%.^{14,15} During the similar respiratory infection of SARS-CoV in 2003, Kwan reported the mortality rate of dialysis patients including HD and peritoneal dialysis was 25%.¹⁶ Emilio Sánchez-Álvarez et al analyzed the SARS-CoV-2 infection in patients on renal replacement therapy in Spain. The mortality rate was 23%, and even higher in in-center HD followed by transplant patients.¹⁷ Alberici et al analyzed the short outcomes of 20 kidney transplant patients admitted for SARS-CoV-2 pneumonia. Five kidney transplant recipients died after a median period of 15 days. We can count the mortality rate was at least 20% in kidney transplant patients.¹⁸ Considering the observation time of both papers was relatively short with one paper less than a month and the other one 15 days, the real mortality rate of COVID-19 MHD patients is probably around 20%–30%.

The survival curve of IHD groups seemed to be flatter; but the log-rank test, which was to compare the survival distributions of two groups, did not reveal any significant differences between the two modalities ($P = .1000$ shown in Figure 2). And also the

multivariate Cox regression analysis showed the HD modality was not a risk for death. The outcome might be influenced by the severity of illness, and our data showed the BSRRT group had relatively higher percentage of patients with symptom of fatigue at the onset of COVID-19 (62.5% vs 36.51%, $P = .0331$), with more bilateral CT abnormalities (96% vs 76.47%, $P = .0496$) and with more patients treated with steroids (25% vs 5.45%, $P = .0199$) (Tables 1–4). The results might imply that although all the patients were diagnosed as noncritical COVID-19 MHD patients, still during the individualized treatment for every individual patient, the attending nephrologists tended to choose BSRRT for relatively severe patients. These findings may imply that even the illness of the BSRRT was relatively severe, still there was no significant difference in survival time and death rates between two groups.

It may be unrealistic to assume that a single decision in the complex care of a COVID-19 MHD patient could significantly influence survival, especially with the fact that until now no certain treatment has been approved to be effective to SARS-CoV-2 infection.¹⁹ Mortality in the COVID-19 MHD patients was likely to be influenced by several factors unrelated to dialysis modality. In the covariate Cox regression analysis, the heart injury and liver injury during the treatment and the treatment of steroids showed significant influence on mortality, meaning that the use of steroids, the occurrence of heart and liver injury were the risk factors for death. But that results could also be argued that the reason for the use of steroids was because of the relatively severe illnesses. And most of the dead patients may have multiple organ dysfunctions including heart and liver failure at the end stage of the disease.

As a modified new dialysis modality, the overall treatment complete rate was 100%. A few complications during therapy were noted. Two of 25 patients had muscle cramps treated by temporary reduction in the ultrafiltration rate. One of 25 patients had mild hyperkalemia (5.8 mg/dL) treated by oral potassium binders and we arranged another session of BSRRT. The specific dialysis-related parameters of all the BSRRT patients are listed in Table 5. The medium therapy time and frequency was 4 hours and three times per week. The medium therapy dose was 70.15 mL/kg/h. It also should be noted that other dialysis-related factors have not been analyzed, including the timing of initiation, the total time of BSRRT and IHD therapy, the standard of monitoring, and choice of membranes.²⁰ Of course, a myriad of other conditions and their treatments (eg, basic nutrition conditions, nutrition support, family support) also may limit the specificity of an intervention such as a change in dialysis modality.

To our knowledge, our study is the first to present a new modified HD modality used in pandemic COVID-19 public health crisis status and presented the detailed HD parameters. And also it is the first study to try to compare the modified HD modality with the conventional IHD therapy of COVID-19 MHD patients. Until now, no paper of the HD modality comparison on COVID-19 MHD patients has been published. At the same time, it is also a multicenter study with the cooperation of all the dialysis centers in Wuhan. In addition to that, this study also provides possibilities of special dialysis modality for MHD patients in other similar disasters such as earthquakes, volcanoes, or hurricanes.

Our study has several potential limitations. First, the study population was restricted to mild COVID-19 MHD patients initially without cardiac complications, so our results may not be generalizable to all MHD patients with COVID-19. Second, it could be argued that with the limited sample size of both groups, we might underestimate the outcome differences, although that could be excused by the fact the total number of diagnosed COVID-19 patients is limited⁵ and also because BSRRT was a new HD modality served mainly for the urgency of the public health crisis, attending nephrologists were relatively cautious. Repetition with a larger sample size and longer follow-up is needed before clear clinical decisions could be made based on our data. Third, in multicenter studies in a public health crisis, the thorough data collection of dialysis treatment prescription and delivered dose was difficult. Fourth, the time of follow-up was still very short; longer observation and analysis should be done to have a more definite conclusion. Finally, it is a retrospective observational study instead of a prospective interventional study. It cannot give a high evidence support of causative conclusion. Better solid evidence could be made if a prospective interventional study could be designed and conducted.

5 | CONCLUSION

In conclusion, our results showed bed-sided short-duration renal replacement therapy is a safe hemodialysis modality. Additionally, the fact that data analysis did not suggest a clear survival benefit of one modality, we think bed-sided short-duration renal replacement therapy could be an option to treat noncritical novel coronavirus infection (coronavirus disease 2019) in maintenance hemodialysis patients in a health care crisis status. It provides another possibility of being used as a substitution for intermittent hemodialysis if needed in a public health crisis even after natural disasters. Still, further prospective studies with longer follow-up to confirm the effect of

BSRRT on clinical outcomes in maintenance hemodialysis patients are necessary.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

AUTHOR CONTRIBUTIONS

Yanglin Hu and Fei Xiong conceived and designed the study. Yanglin Hu drafted the manuscript and analyzed the data. Can Tu, Yuting Song, and Mengliang Zhou collected the data. Wen-Li Chen, Jun-Wu Dong, Xiao-Hui Wang, Dan Luo, Ming Shi, Xiao-Hui Wang, Chun Zhang, and Fei Xiong provided additional guidance for data collection and analysis. All authors critically revised the manuscript for important intellectual content and approved the final version for publication.

ETHICS STATEMENT

The institutional ethics board of Wuhan No. 1 Hospital approved this study. We conducted direct communication with patients or their families as much as possible. Written informed consent was waived because of the rapid emergence of this infectious disease, and verbal consent obtained.

ORCID

Yanglin Hu  <https://orcid.org/0000-0002-1130-3467>

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