Prolonged Intermittent Renal Replacement Therapy for Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome

Juan C. Ramirez-Sandoval^a Jorge E. Gaytan-Arocha^a Pedro Xolalpa-Chávez^a
Juan M. Mejia-Vilet^a Mauricio Arvizu-Hernandez^a Eduardo Rivero-Sigarroa^b
Carlos Torruco-Sotelo^b Ricardo Correa-Rotter^a Olynka Vega-Vega^a

^aDepartment of Nephrology and Mineral Metabolism, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico; ^bDepartment of Intensive Care, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Keywords

Renal failure · SARS-CoV-2 · Acute respiratory distress syndrome · Hybrid therapies · Sustained low-efficiency dialysis

Abstract

Introduction: Patients with acute respiratory distress syndrome (ARDS) secondary to COVID-19 frequently develop severe acute kidney injury (AKI). Although continuous renal replacement therapy is the standard of care for critically ill patients, prolonged intermittent renal replacement therapy (PIRRT) may be a feasible option. We aimed to describe the tolerability and security of PIRRT treatments in COVID-19 patients with ARDS who required mechanical ventilation and developed severe AKI. **Methods:** We prospectively analyzed patients who underwent PIRRT treatments at a COVID-19 reference hospital in Mexico City. Intradialytic hypotension was defined as a systolic blood pressure decrease of ≥ 20 mm Hg or an increase of 100% in vasopressor dose. **Results:** We

identified 136 AKI cases (60.7%) in 224 patients admitted to the intensive care unit. Among them, 21 (15%) underwent PIRRT (130 sessions) due to stage 3 AKI. The median age of the cohort was 49 (range 36–73) years, 17 (81%) were male, 7 (33%) had diabetes, and the median time between symptoms onset and PIRRT initiation was 12 (interquartile range [IQR] 7–14) days. The median of PIRRT procedures for each patient was 5 (IQR 4–9) sessions. In 108 (83%) PIRRT sessions, the total ultrafiltration goal was achieved. In 84 (65%) PIRRT procedures, there was a median increase in norepinephrine dose of $+0.031$ mcg/kg/min during PIRRT (IQR 0.00 to $+0.07$). Intradialytic hypotensive events occurred in 56 (43%) procedures. Fifteen (12%) PIRRT treatments were discontinued due to severe hypotension. Vasopressor treatment at PIRRT session onset (OR 6.2, 95% CI 1.4–28.0, p : 0.02) and a pre-PIRRT lactate ≥ 3.0 mmol/L (OR 4.63, 95% CI 1.3–12.8, p : 0.003) were independently and significantly associated with the risk of hypotension during PIRRT. During follow-up, 11 patients (52%) recovered from AKI and respiratory failure and 9 (43%) died. Several adaptations to our PIRRT protocol dur-

ing the COVID-19 outbreak are presented. **Conclusions:** PIRRT was feasible in the majority of COVID-19 patients with ARDS and severe AKI, despite frequent transitory intradialytic hypotensive episodes. PIRRT may represent an acceptable alternative of renal replacement therapy during the COVID-19 outbreak.

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Introduction

As the COVID-19 pandemic unfolds in several countries, a high number of patients with severe acute kidney injury (AKI) secondary to COVID-19 pneumonia have become evident. Although continuous renal replacement therapy (CRRT) is the treatment of choice for hemodynamically unstable critically ill patients, its use implies a higher complexity, more extensive training and time-consuming procedures for nursing staff, the need for continuous anticoagulation, availability of multiple CRRT equipment, and significantly higher costs [1, 2]. Other treatments, as sequential extracorporeal therapies, are an option for COVID-19 patients with multiple organ failure, as they provide all forms of organ support [3, 4] and reduce the level of various inflammatory mediators [5]. Nevertheless, these therapies are not available in many institutions.

Prolonged intermittent renal replacement therapy (PIRRT), also known as sustained low-efficiency dialysis or slow extended daily dialysis, may be an option for critically ill COVID-19 patients given its advantages related to flexible treatment schedules, acceptable hemodynamic tolerability, less nursing time, and lower costs than CRRT [2]. Nevertheless, PIRRT could be inconvenient for COVID-19 patients, who commonly exhibit an exuberant inflammatory response, severe hemodynamic instability, and hypercoagulability. In this article, we describe our experience of 130 PIRRT treatments in 21 COVID-19 patients with acute respiratory distress syndrome (ARDS) who required mechanical ventilation and developed severe AKI, most of them with hemodynamic instability. Therefore, we present several adaptations to our PIRRT protocol after the COVID-19 outbreak.

Materials and Methods

This is a single-center, prospective, observational study performed at the Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, a tertiary reference hospital designated to treat exclusively patients with COVID-19 in Mexico City since March

16, 2020. From this date to June 24, 2020, we prospectively analyzed all PIRRT treatments performed in COVID-19 subjects. SARS-CoV-2 infection was confirmed by RT-PCR in all the cases. The Human Research and Ethics Committees of our institution approved our study (reference number NMM-3325-20-20-1). Written informed consent was waived due to the observational nature of the study.

All the included patients had moderate to severe ARDS ($\text{PaO}_2/\text{FiO}_2 \leq 200$ mm Hg) according to the Berlin ARDS definitions [6] and were receiving mechanical ventilation. The choice between PIRRT and CRRT as the initial renal replacement therapy (RRT) was made at the discretion of the consulting nephrologist who considered, in addition to the clinical characteristics of each patient, the shortage of medical personnel, nursery staff, and RRT supplies during the start of the pandemic. Each patient received ≥ 3 treatment sessions with high-flux dialyzers (clearance Qb 200 mL/min, urea 192, effective surface 1.9 m^2 , DIAPES®, Bellco, Italy). All hemodialysis machines used were 4008 S (®Fresenius, Germany). All consulting nephrologists prescribed a total fluid removal per hour of <400 mL/h per institutional protocol. We collected data on age, sex, previous comorbidities, symptoms from onset to hospital admission and to PIRRT initiation, laboratory values on PIRRT initiation, treatment (vasoconstrictive agents), and living status.

The outcomes included successful PIRRT according to dialytic and ultrafiltrate goals prescription, events of intradialytic hypotension, system clotting or other adverse events during the PIRRT procedure, mortality, and renal recovery. Intradialytic hypotension was defined as a systolic blood pressure decrease ≥ 20 mm Hg or an increase of 100% in baseline vasopressor dose [7]. Severe intradialytic hypotension was defined as an intradialytic hypotensive episode that required PIRRT interruption. Renal recovery was defined as RRT independence >14 days after intensive care unit (ICU) discharge.

We expressed categorical variables as numbers (percentages) and continuous variables as mean $\pm$ standard deviation (SD) or median (interquartile range [IQR]), as appropriate. Comparison between groups was performed with a t test or the Mann-Whitney test for continuous variables and χ^2 test or Fisher's test for categorical variables. Variables associated with intradialytic hypotensive episodes with a p value below 0.1 in the univariate analysis were selected for inclusion into a multivariate logistic regression model using forward stepwise selection. Statistical analysis and graphics were performed with SPSS 21.0 software (SPSS Inc., Chicago, IL, USA) and GraphPad Prism 5 (San Diego, CA, USA), respectively. The results were considered statistically significant when $p < 0.05$.

Results

We identified 224 COVID-19 patients admitted to our ICU; 136 (60.7%) of them developed hospital-acquired AKI, and among them, 39 (29%) had stage 3 AKI according to KDIGO definitions [8]. In these patients, 21 (15%) initiated PIRRT. We excluded patients who were treated initially with CRRT instead of PIRRT ($n = 3$). The rest of stage 3 AKI cases were no candidates for RRT given their clinical status (see Fig. 1).

Fig. 1. Flowchart of the patients included. AKI, acute kidney injury; ICU, intensive care unit; CRRT, continuous renal replacement therapy; RRT, renal replacement therapy; PIRRT, prolonged intermittent renal replacement therapy.

We analyzed 130 PIRRT sessions administered to 21 patients. The median age was 49 (IQR 45–59, range 36–73) years, 17 (81%) were male, 7 (33%) had diabetes, and 8 (38%) had a previous diagnosis of systemic hypertension. The median BMI was 31 (IQR 28–36, range 22–51) kg/m², median SOFA score was 10 (IQR 9–11) points, and median time between symptoms onset and PIRRT initiation was 12 (IQR 7–14) days. All but 1 patient had fever ($\geq 38^{\circ}\text{C}$) within 24 h before PIRRT initiation. PIRRT was started 72 h after intubation in all patients, except in 3 who had life-threatening dialysis indications (hyperkalemia and severe mixed acidosis) and who started therapy earlier at their admission. Other clinical characteristics are shown in Table 1.

The median of PIRRT procedures for each patient was 5 (IQR 4–9) (Table 2). In 108 (83%) PIRRT sessions, the ultrafiltration goal was achieved. The duration of PIRRT was 6–8 h in 91 treatments (70%), as planned. In 17 (13%) sessions, the PIRRT procedure was extended 2–4 additional hours in addition to the original prescription to complete the ultrafiltration goal. In 84 (65%) PIRRT procedures, in which patients were initially under vasopressor therapy with norepinephrine, there was a median increase in norepinephrine dose of +0.031 mcg/kg/min during PIRRT (IQR 0.001 to +0.072), and 8 (6%) patients required norepinephrine infusion during the PIRRT session.

Intradialytic hypotensive events occurred in 56 (43%) procedures. Intradialytic hypotensive episodes were identified promptly in the majority of episodes and treated with 2 maneuvers: increasing norepinephrine dose

Table 1. Clinical characteristics of patients on the day of PIRRT initiation

Subjects' characteristics at PIRRT session onset (n = 21)	
Serum Cr, mg/dL	4.6 (4.2–5.8)
Blood urea nitrogen, mg/dL	55 (40–67)
Urine output, mL/d	189 (45–390)
Anuric patients (<100 mL/d), n (%)	7 (33)
PaO ₂ /FiO ₂	123 (102–151)
Hemoglobin, g/dL	10.6 (11.2–12.7)
WBC, 10 ³ /μL	11.7 (8.0–13.6)
Lymphocytes, 10 ³ /μL	0.45 (0.39–0.66)
Sodium, mEq/L	139 (137–142)
Potassium, mEq/L	4.6 (4.3–5.0)
C-reactive protein, mg/L	35 (19–61)
D-dimer, ng/mL	3,076 (2,019–5,662)
Ferritin, ng/mL	1,038 (513–1,350)
<i>Arterial blood gas</i>	
pH	7.22 (7.19–7.28)
pCO ₂ , mm Hg	55.1 (46.4–63.0)
HCO ₃ , mEq/L	23 (22.1–26.2)
Arterial lactate, mg/dL	1.3 (1.8–2.3)
<i>Ventilator parameters</i>	
Plateau pressure, cm/H ₂ O	27 (23–29)
Static compliance, cm/H ₂ O	34 (27–37)
PEEP, cm/H ₂ O	14 (14–16)
Prone positioning, n (%)	4 (19)
Vasopressor use, n (%)	21 (100)
Vasopressor dose, μg/kg/min	0.08 (0.1–0.12)
PIRRT, prolonged intermittent renal replacement therapy; PEEP, positive end-expiratory pressure.	

Table 2. Characteristics of the PIRRT sessions

Characteristic	
Number of PIRRT sessions, <i>n</i>	130
Number of PIRRT sessions per patient, <i>n</i>	5 (4–9)
Treatment time, h [IQR]	6 (6–8)
Treatments that achieved full prescription time and ultrafiltrate goal, <i>n</i> (%)	102 (77)
Total duration of dialyzer effluent exposure, h [IQR]	4 (4–4)
Weight-adjusted ultrafiltration rate initially prescribed, mL/kg/h	3.8 (2.8–4.9)
Total fluid removal per session, L	2.5 (2.0–2.5)
Fluid removal per hour, mL/h	313 (125–416)
Dialyzer blood flow rate, mL/min	200 (200–250)
Dialyzer blood flow rate, mL/kg	300 (300–500)
Vasopressor therapy before PIRRT initiation, <i>n</i> (%)	84 (65)
Vasopressor therapy after PIRRT initiation, <i>n</i> (%)	8 (6)
Initial NOR dose, µg/kg/min	0.06 (0.03–0.14)
Final NOR dose, µg/kg/min	0.09 (0.06–0.16)
Initial HR, bpm	96 (77–111)
Final HR, bpm	101 (84–110)
Initial SBP, mm/Hg	116 (105–130)
Final SBP, mm/Hg	108 (97–121)
Initial DBP, mm/Hg	58 (52–65)
Final DBP, mm/Hg	58 (54–62)
Treatments discontinued due to severe hypotensive episode, <i>n</i> (%)	15 (12)
Treatments in which clotting occurred at least once, <i>n</i> (%)	17 (13)
Treatments performed using heparin anticoagulation, <i>n</i> (%)	116 (89)
Mean heparin infusion rate per hour, U/h	500 (500–500)
Enoxaparin prescription, <i>n</i> (%)	68 (52)

Pertreatment analysis. Bpm, beats per minute; PEEP, positive end-expiratory pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; NOR, norepinephrine; PIRRT, prolonged intermittent renal replacement therapy; IQR, interquartile range.

Fig. 2. Forest plot of risk factors associated with at least one intradialytic hypotensive episode in the univariate model (**a**) and retained in the multivariate model (**b**). +No-vasopressor at PIRRT session onset was the reference.

Table 3. Characteristics of PIRRT procedures according to the occurrence of intradialytic hypotensive events

Characteristic	Hypotension during PIRRT session (<i>n</i> = 56)	No hypotension during PIRRT session (<i>n</i> = 74)	<i>p</i> value
Total time of PIRRT, h	7.5 (6–8)	6 (5–8)	0.002
Total duration of dialyzate effluent exposure, h	4 (4–4)	4 (4–4)	1.00
Blood flow rate, mL/min	200 (200–300)	200 (200–200)	0.15
Dialyzate flow rate, mL/kg	300 (300–500)	300 (300–300)	0.081
Hb, g/dL	10.3±2.2	10.3±2.9	0.91
WBC, 10 ³ /μL	13.6 (10.3–16.9)	11.5 (8.8–14.5)	0.022
Na, mEq/L	135 (133–138)	135 (134–138)	0.42
K, mg/dL	4.4±0.7	4.3±0.7	0.92
Ferritin, ng/mL	520 (330–1,342)	953 (519–1,336)	0.086
Lactate, mg/dL	2.2 (1.7–2.9)	1.8 (1.3–2.4)	0.071
Lactate ≥3.0 mg/dL, <i>n</i>	9 (21%)	3 (4%)	0.029
D-dimer, ng/mL	3,906 (2,126–6,362)	4,294 (2,624–8,424)	0.28
Prone position, <i>n</i>	11 (19)	18 (24)	0.52
PEEP, mL/cm/H ₂ O	12 (8–14)	12 (8–14)	0.99
Static compliance, mL/cm/H ₂ O	35 (29–44)	32 (25–43)	0.29
pH	7.25±0.07	7.29±0.09	0.10
HCO ₃	22.1±3.1	23.1±3.5	0.10
pCO ₂	49 (40–57)	50 (40–58)	0.92
Accumulated net fluid balance, mL	96±1,655	−447±1,025	0.025
Total UF goal, L	2.5 (2–3.0)	2.0 (2.0–2.5)	0.26
Initial UF rate per hour prescribed, mL/h	317±131	326±162	0.35
Initial UF rate adjusted weight, mL/kg/h	3.8±1.5	3.9±2.2	0.85
UF rate per hour accomplished, mL/h	293±134	368±139	0.004
UF rate-adjusted weight accomplished, mL/kg/h	3.6±1.4	3.7±1.6	0.72
Vasopressor therapy, <i>n</i> (%)	47 (56)	37 (44)	0.001
Initial NOR, μg/kg/min	0.05 (0.01–0.12)	0.05 (0.03–0.14)	0.31
Final NOR, μg/kg/min	0.11 (0.07–0.20)	0.06 (0.03–0.15)	0.017
Change in NOR dose, μg/kg/min	+0.07 (0.04–0.09)	0 (0–0.01)	<0.001
Temperature, °C	37 (36.8–38.6)	37 (36.5–37.6)	0.35
Initial SBP, mm Hg	120±25	119±18	0.64
Initial DBP, mm Hg	60±11	59±11	0.42
Final SBP, mm Hg	110±22	111±19	0.55
Final DBP, mm Hg	62±17	59±11	0.22
Initial HR, bpm	97 (79–113)	90 (65–105)	0.016
Final HR, bpm	105 (91–127)	95 (77–106)	0.019

Data are presented as mean ± standard deviation, median (interquartile range), or *n* (%). All variables are shown at the PIRRT session onset. NOR, norepinephrine; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; PIRRT, prolonged intermittent renal replacement therapy; PEEP, positive end-expiratory pressure.

(54/56, 96%) and reducing fluid removal rate by decreasing total ultrafiltrate (10/56, 18%) or by increasing session duration (46/56, 82%). Fifteen (12%) PIRRT treatments were discontinued before reaching the ultrafiltration goal due to severe intradialytic hypotension. Other causes of PIRRT discontinuation were recurrent dialysis system clotting, arrhythmia, and refractory hypoxemia in 5, 1, and 1 procedure, respectively. Two patients were switched to CRRT due to severe hypotension after 2 consecutive PIRRT treatments failed on subsequent days.

The median (IQR) proportion of intradialytic hypotensive events per each patient (the frequency of hypotensive events divided by the total number of PIRRT treatments per patient) was 0.4 (0.1–0.7). Men had a higher proportion of intradialytic hypotensive events than women (0.64 [0.30–0.73] vs. 0.40 [0.11–0.60], *p*: 0.032). The characteristics of PIRRT sessions complicated by intradialytic hypotensive events compared to those without hypotensive episodes are displayed in Table 3. As it is shown, PIRRT sessions complicated by intradialytic hy-

Table 4. Suggestion for PIRRT in COVID-19 patients with ARDS

PIRRT-related factor	Suggestion	Rationale according to our observational data
“Early” placement of vascular access	In high-risk patients for RRT, place a CVC before adopting prone position	During the first weeks of pandemic, urgent CVC placements were complicated by the prone position of patients with severe ARDS in our cohort ($n = 4$). Turning to supine position for timely CVC insertion was not possible in 2 patients; fortunately, PIRRT could be delayed without severe complications. Although safe ultrasound-guided CVC placement in prone position has been described [9], we decided to adopt an “early” placement of CVC before adopting prone position in those subjects with mechanical ventilation and high risk for RRT
Timing for initiation of PIRRT	Reduce net positive fluid balance until a complete resuscitation fluid is confirmed. Consider high insensible fluid losses related to persistent fever. Bedside ultrasound-guided volume could be useful to assess fluid status	In our ICU, a strategy of conservative fluid management has been employed in the majority of patients according to the recommendations for ARDS. In this regard, the median cumulative fluid balance from admission to PIRRT initiation was 3.56 (range 1.8–6.7) L. Nevertheless, cumulative fluid balance charts were frequently inaccurate compared to clinical and ultrasound assessment given high insensible fluid losses related to persistent fever. For example, 12 non-PIRRT patients with stage3 AKI and anuria were frankly depleted by ultrasound-guided volume assessment and responded to fluid repletion. We tried to delay PIRRT initiation until a complete resuscitation was documented, including ultrasound volume markers when possible, allowing time to assess the response to fluids and furosemide test
Limit COVID-19 exposure	If possible, limit hemodialysis staff exposure	Aiming to limit exposure among hemodialysis staff, and to limit the use of personal protective equipment, patients with COVID-19 and AKI who required PIRRT were placed close together in the ICU when possible. Thus, one nurse simultaneously delivered dialysis to more than one patient in adjoining beds for a maximum period of 4–6 h; when the PIRRT is longer than that, a second nurse would come to replace the first one
Prothrombotic complications	Use of systemic anticoagulation and regional anticoagulation	Circuit thrombotic events were frequent during the first 2 weeks of the COVID-19 outbreak. The institutional protocol adopted the use of systemic anticoagulation (enoxaparin SC 0.5 mg/kg/d), and during PIRRT, we added regional anticoagulation using unfractionated heparin (500 U/h). Anti-factor Xa activity was measured every 4 days with a target anti-Xa activity of 0.6–1.0
Severe acidemia	Increased dialyzate base yet avoid sudden pH normalization	Permissive hypercapnia caused by low tidal volume ventilation (6 mL/kg of predicted body weight) was associated to arterial pH below 7.25 before PIRRT initiation in the majority of patients (11/14), despite prescription of large volumes of bicarbonate in all patients (range 100–250 mEq/d [11]). In general, we increased dialyzate base +4 mEq/L (32 mEq/L) and prescribed dialyzate flows of 300 mL/min for no more than 4 h, intended to achieve a pH > 7.25, avoiding sudden pH normalization

PIRRT, prolonged intermittent renal replacement therapy; CVC, central venous catheter; RRT, renal replacement therapy; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; ICU, intensive care unit.

potensive events had longer duration, less fluid removal per hour, and a higher increase in vasopressor dose, and occurred more frequently in male patients with higher WBC counts, heart rate frequencies, and arterial lactate concentrations. We performed a multivariate analysis of variables associated with intradialytic hypotensive events using the variables shown in Figure 2. Vasopressor at PIRRT session onset (OR 6.2, 95% CI 1.4–28.0, $p:0.02$) and a pre-PIRRT lactate ≥ 3.0 mmol/L (OR 4.63, 95% CI 1.3–12.8, $p:0.003$) were independently and significantly associated with the risk of hypotension during PIRRT.

Circuit thrombotic events were frequent during the first 2 weeks of the COVID-19 outbreak. In the first 30 PIRRTs, 7/30 (23%) clotting events occurred at least once. Two central venous catheters were removed due to irreversible occlusion of the lumen by thrombus. Nurse and

laboratory staff shortages prevented the use of total coagulation with unfractionated heparin since adequate monitoring of coagulation times was not possible. Therefore, the institutional protocol adopted the use of systemic anticoagulation (enoxaparin SC 0.5 mg/kg/day), and during PIRRT, we added regional anticoagulation using unfractionated heparin (500 U/h). Anti-factor Xa activity was measured every 4 days 3–4 h after enoxaparin application with a target anti-Xa activity of 0.6–1.0 UI/mL [10]. After these maneuvers, the proportion of treatments in which clotting occurred at least once decreased from 23 to 10% (10/100, $p < 0.001$). After double anticoagulation, 2 cases presented minor bleeding which resolved after discontinuation of enoxaparin. We introduced other changes in our PIRRT protocol during the COVID-19 outbreak to maximize resources and to address the spe-

cific needs of COVID-19 patients, which are shown in Table 4.

During follow-up, 11 patients (52%) recovered from AKI and respiratory failure, 9 (43%) patients died, and 1 (5%) patient is still hospitalized at the time of writing this report, yet he has recovered renal function and, subsequently, PIRRT has already been discontinued. In those patients who recovered renal function (12/21), the median number of PIRRT sessions was 5 (IQR 4–10) and the median time of follow-up was 28 (14–62) days. None of the deaths were directly or indirectly related to adverse events during the PIRRT session.

Discussion/Conclusion

In the last 14 weeks, our ICUs unexpectedly faced multiple challenges for delivering timely RRT in multiple extremely ill patients, including shortages of nursing staff, vital equipment, and hemodialysis machines. Our main findings are that (1) PIRRT sessions were feasible in almost 85% of procedures, (2) intradialytic hypotensive episodes were a frequent event in these patients and were mainly related to inflammatory status and organ hypoperfusion assessed by arterial lactate and vasopressor use, (3) the majority of the hypotensive episodes were identified and successfully treated with reduction of planned fluid removal during PIRRT session and increasing session duration, and (4) systemic anticoagulation with low-molecular-weight heparin and regional anticoagulation of the PIRRT system reduced the high incidence of the circuit and access thrombosis observed in ICU patients with COVID-19 infection.

Contrary to the initial reports of a very low incidence of AKI associated to SARS-CoV-2 [12], recent reviews estimated an AKI occurrence between 8.3 and 23% and a frequency of RRT requirement of 14.6–58.3% in critically ill COVID-19 patients who developed AKI [13, 14]. In our cohort, we found a high AKI occurrence of 60.7% during the ICU stay, and among them, severe AKI (stage 3) occurred in almost one-third of cases. These discrepancies between our results and others could be explained by the strict application of KDIGO criteria, a high prevalence of diabetes and hypertension, the severity of ARDS, and the longer stay in the ICU. Nevertheless, the proportion of critically ill COVID-19 cases needing RRT in all patients admitted to the ICU was <10%, which is lower than previous projections of 25% suggested by other authors [15].

Survival data of COVID-19 patients who needed RRT are incomplete in the literature so far published. Yang et

al. [16] and Zhou et al. [17] showed a mortality in severely ill patients treated with CRRT of 89% ($n = 8/9$) and 100% ($n = 10/10$), respectively. In a recent meta-analysis, CRRT initiation was a poor prognosis factor in severe COVID-19, given that 15.6% of non-survivors of COVID-19 received CRRT compared to 0.4% of survivors [18]. In our center, we observed a mortality of <50% in patients treated with PIRRT. A hopeful observation is that more than half of the patients treated with PIRRT survived, recovered kidney function, and were discharged within 28 days after RRT initiation. It is conceivable that our survival outcomes are most likely the result of many factors, including ICU team's competition and performance, but our data provide reassurance of continuing to use PIRRT in critically ill COVID-19 patients.

The frequency of intradialytic hypotensive episodes observed was within the range of other non-COVID-19 cohorts in the ICU treated with PIRRT, which is between 17 and 57% [19–23]. The requirement of any dose of vasopressor or pre-PIRRT elevated arterial lactate, both of which are related to the severity of COVID-19 infection, was strongly related to hypotensive episodes. Despite all the adopted measures to avoid intradialytic hypotension in this cohort, there were no differences in PIRRT prescription between those PIRRT procedures which presented hypotensive episodes and those without this complication. Extending the total time of PIRRT procedures or decreasing the ultrafiltrate rate to <400 mL/h in hemodynamically unstable patients was not effective in decreasing the risk of hypotensive events, as it has been described in other series [24]. Although CRRT modality is presumed to have the least impact on hemodynamic stability, the superiority of CRRT over PIRRT to prevent hypotensive episodes and other outcomes such as renal recovery and mortality is controversial [25, 26]. The advantage of performing several dialysis procedures with short nursing staff and at low cost constitutes a very important advantage of PIRRT over CRRT in our center. For example, at our hospital, the CRRT supplies cost is approximately 17-fold higher than that of the PIRRT supplies (USD 455 vs. USD 27, respectively). Nevertheless, we believe that our COVID-19 patients with multiorgan failure demand better modalities of RRT that achieve hemodynamic stability, decrease adverse events during treatments, and provide alternative ways to improve clinical outcomes, for example, the removal of cytokines during “the cytokine storm period” related to SARS-CoV-2 infection [5].

Even peritoneal dialysis is a common choice of replacement therapy in Mexico, and few authors have suggested this modality as a feasible option during the CO-

VID-19 outbreak [27, 28], yet it was not achievable due to the need for prone positioning in most of the COVID-19 patients with ARDS. Other factors that may have made it not reasonable to adopt this strategy at our center would have been an insufficient number of trained staff, exposure risk associated with frequent fluid exchanges, and the difficulties for timely peritoneal catheter placement.

Our study has limitations. The observational design of this study limits its generalizability, the lack of significant differences in many clinical characteristics associated with adverse events could be due to the small number of patients, and our suggestions must be validated in prospective and multicenter trials to confirm our hypothesis. So far, we did not find studies about PIRRT feasibility in critically ill COVID-19 patients with ARDS and severe AKI.

In conclusion, PIRRT may represent an acceptable alternative for other centers with circumstances similar to our managing COVID-19 patients with ARDS and severe AKI. In these extraordinary circumstances, PIRRT therapy was feasible in the majority of our patients who exhibited an exuberant inflammatory response, severe hemodynamic instability, and hypercoagulability.

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Statement of Ethics

Patients' informed consent was obtained, and the protocol was approved by the institutional review board (number protocol NMM-3325-20-20-1).

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Conflict of Interest Statement

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Author Contributions

All authors conceived and designed the study. All authors performed the inclusion of subjects and prospective follow-up. J.C.R.S., J.E.G.A., P.X.C., J.M.M.V., M.A.H., E.R.S., C.T.S., R.C.R., and O.V.V. analyzed the data and reviewed the results. J.C.R.S., J.M.M.V., R.C.R., and O.V.V. wrote the manuscript. All authors revised the manuscript.

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