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The role of peritoneal dialysis in the treatment of acute kidney injury in neurocritical patients: a retrospective Brazilian study

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Abstract

Background: Acute kidney injury (AKI) occurs frequently in the neurocritical intensive care unit and is associated with greater morbidity and mortality. AKI and its treatment, including acute kidney replacement therapy, can expose patients to a secondary greater brain injury. This study aimed to explore the role of peritoneal dialysis (PD) in neurocritical AKI patients in relation to metabolic and fluid control, complications related to PD and outcome.

Methods: Neurocritical AKI patients were treated by PD (prescribed Kt/V = 0.40/session) using a flexible catheter and a cycler and lactate as a buffer.

Results: A total of 58 patients were included. The mean age was 61.8 ± 13.2 years, 65.5% were in the intensive care unit, 68.5% needed intravenous inotropic agents, 72.4% were on mechanical ventilation, APACHE II was 16 ± 6.67 and the main neurological diagnoses were stroke (25.9%) and intracerebral haemorrhage (31%). Ischaemic acute tubular necrosis (iATN) was the most common cause of AKI (51.7%), followed by nephrotoxic ATN AKI (25.8%). The main dialysis indications were uraemia and hypervolemia. Blood urea and creatinine levels stabilised after four sessions at around 48 ± 11 mg/dL and 2.9 ± 0.4 mg/dL, respectively. Negative fluid balance and ultrafiltration increased progressively and stabilised around 2.1 ± 0.4 L /day. Weekly delivered Kt/V was 2.6 ± 0.31. The median number of high-volume PD sessions was 6 (4–10). Peritonitis and mechanical complications were not frequent (8.6% and 10.3%, respectively). Mortality rate was 58.6%. Logistic regression identified as factors associated with death in neurocritical AKI patients: age (odds ratio (OR) = 1.14, 95% confidence interval (CI) = 1.09–2.16, $p = 0.001$), nephrotoxic AKI (OR = 0.78, 95% CI = 0.69– 0.95, $p = 0.03$), mechanical ventilation (OR = 1.54, 95% CI = 1.17–2.46, $p = 0.01$), intracerebral haemorrhage as main neurological diagnoses (OR = 1.15, 95% CI = 1.09–2.11, $p = 0.03$) and negative fluid balance after two PD sessions (OR = 0.94, 95% CI = 0.74–0.97, $p = 0.009$).

Conclusion: Our study suggests that careful prescription may contribute to providing adequate treatment for most neurocritical AKI patients without contraindications for PD use, allowing adequate metabolic and fluid control, with no increase in the number of infectious, mechanical and metabolic complications. Mechanical ventilation, positive fluid balance and intracerebral haemorrhage were factors associated with mortality, while patients with nephrotoxic AKI had lower odds of mortality compared to those with septic and ischaemic AKI. Further studies are needed to investigate better the role of PD in neurocritical patients with AKI.

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Keywords
Acute kidney injury, cerebral haemorrhage, neurocritical intensive care, peritoneal dialysis, stroke, subarachnoid haemorrhage, traumatic brain injury

Introduction

The incidence of acute kidney injury (AKI) in neurocritical patients varies from 11.6% to 38% according to their disease, which includes traumatic brain injury, subarachnoid haemorrhage, stroke and intracerebral haemorrhage.[1,2] The main reasons for the development of AKI in neurocritical patients are infections, hypovolemia associated with bleeding and nephrotoxicity.[3,4]

In neurocritical patients, AKI and its treatment can alter the kidney–brain axis, exposing patients undergoing acute kidney replacement therapy (AKRT) to greater injury.[4–6] AKRT can decrease neurotoxicity and delirium by clearing nitrogen products, sedatives, antibiotics, as well as by correcting acidosis, hyperkalaemia and fluid balance.[5,6] However, it may cause secondary brain damage by inducing or accentuating cerebral oedema, with the resulting elevation in intracranial pressure (ICP) and cerebral ischaemia.[1]

Intermittent and continuous therapies have been shown to be equally effective in terms of dependence on dialysis and mortality, but the mechanism and speed at which the two techniques achieve blood clearance differ.[7] In neurocritical care, abrupt changes in osmolarity and volemia secondary to effective therapy affect the kidney–brain connection, altering cerebral blood flow, cerebral perfusion pressure and on the whole modifying ICP.[1] For these reasons, peritoneal dialysis (PD) and continuous kidney replacement therapy (CKRT) could achieve optimal clearance control and potentially reduce the risk of secondary brain injury. Case reports suggest that the use of PD as a continuous therapy would not lead to acute neurological changes in ICP or brain density and achieve successful control of fluid, electrolytes and acid–base balance without the need for anticoagulation.[8–10] However, PD is not used in these patients currently due to the development and availability of other intermittent and continuous AKRT, despite the fact there is no evidence of their superiority of PD, particularly in selected patients.[11,12]

According to Brazilian studies, currently, between 3% and 19% of patients with AKI are on PD as AKRT.[13,14] Two PD modalities have been shown to be successful in AKI: tidal PD (TPD) and high-volume PD (HVPD).[13–18] In HVPD, a method proposed by Ponce, a large volume of dialysate is delivered in short cycles mediated by a cycler (18–22 cycles per day with 30–60 min of dwell time) for 24 continuous hours, 7 days a week, achieving Kt/V urea around 0.4 per session. This achieves adequate metabolic control at 4 days of starting therapy with no differences in mortality compared to patients treated with conventional or prolonged daily haemodialysis (HD).[16–18] Nevertheless, these studies did not report any neurocritical patients in their groups, which is a limitation when extrapolating the findings to these patients.

Given the paucity of evidence in this important area, the aim of this study was first to investigate the in-hospital mortality of neurocritical AKI patients treated with PD; second to determine the metabolic and fluid control; third the complications related to PD; and, finally, to identify the risk factors associated with death.

Methods

Study population

This study is a sub-analysis of a larger retrospective observational study that investigated the epidemiology of AKI and its effect on patient outcomes across time periods.[19] This study was separately approved by the Ethics Committee of Botucatu School of Medicine University Hospital, Sao Paulo, Brazil (protocol 30457414.7.0000.5411). Written informed consent was obtained from all patients or relatives prior to their inclusion in the study. Neurocritical patients who had been consecutively treated by HVPD were evaluated between July 2012 and June 2022. Patients hospitalised with traumatic brain injury, subarachnoid haemorrhage, stroke, intracerebral haemorrhage as the primary diagnosis and with ischemic or nephrotoxic stage 3 AKI according to the KDIGO criteria were eligible for enrolment.[5]

The diagnosis of AKI, and its cause, was determined by a nephrologist in charge of the patient at the time of hospitalisation, by considering the existing standard definitions. Aetiological causes that led to AKI via deficiencies in blood flow to the kidney were classified in the pre renal group, causes that acted via injury to the renal tissue were in the renal group and, finally, causes that resulted in AKI via creating an obstacle to evacuation of urine were placed in the post-renal group. Aetiology of renal AKI was classified as ischemic or nephrotoxic acute tubular necrosis, septic and glomerular or interstitial tubular nephritis. AKI aetiology was also classified as a mixed or uncertain disorder.[3,4,9]

The criteria used for AKRT initiation were as follows: azotaemia (serum urea greater than 200 mg/dL); refractory hyperkalaemia (>6 mmol/L); metabolic acidosis refractory to clinical measures (pH < 7.2); acute pulmonary oedema due to hypervolemia (fluid overload was higher than 5% and impaired gas change, presence of pulmonary rales on physical exam and chest X-ray with signs of volume overload. The chosen method was also determined by the nephrology team after evaluation of the AKRT indication criteria; the contraindications of each method; and the haemodynamic, clinical and catabolic conditions of each

patient, considering the presence of hypervolemia, haemodynamic instability, acute brain injury, intracranial hypertension and hypercatabolism. The methods used included conventional intermittent haemodialysis (IHD), prolonged IHD, continuous venovenous haemodiafiltration (CVVHDF) and PD.[5,17–19]

Exclusion criteria were age under 18 years, chronic kidney disease stages 4 and 5,[20] renal transplantation, pregnancy, other aetiologies of AKI (post-renal and glomerulonephritis) and absolute contraindication for PD (recent abdominal surgery,[17] severe hyperkalaemia with electrocardiogram changes, severe respiratory failure (fraction of inspired oxygen (FiO_2) >70%), acute pulmonary oedema).[20–22] If patients presented any one of these contraindications, they were treated by prolonged HD or CKRT, according to their haemodynamic instability.

Study protocol

Once PD was indicated, catheter implantation was performed by Seldinger's percutaneous technique[21] under prophylactic antibiotic therapy (cefazolin 1 g if hospitalisation time $\leq$ 7 days and vancomycin if > 7 days). All implants were performed by the nephrologists of the dialysis unit.

The PD was performed according to previous studies by Ponce et al. and the International Society for Peritoneal Dialysis (ISPD) guidelines for PD in AKI: 2020 update.[20,22–24] The prescribed Kt/V was 0.4/session, and the total volume ranged from 18 to 32 L/day. Cefazolin was used as a prophylactic antibiotic to cover PD catheter insertion. Patients were treated with continuous PD, and exchanges with Dianeal (Baxter) PD solution (Na = 135 mEq/L, Ca = 3.5 mEq/L, K = 0 mEq/L, Mg = 1.5 mEq/L, lactate = 40 mEq/L, 1.5–2.5% dextrose) were performed using a HOMECHOICE cycler (Baxter). To evaluate the adequacy of the dialysis, delivered Kt/V, ultrafiltration (UF) and fluid balance were calculated daily. Serum osmolality was also calculated once a day.

Baseline body weight was recorded at initial hospital admission. Oliguria was defined as urine output <0.5 mL/kg/h for at least 6 h. The cumulative fluid balance was registered 48 h before starting dialysis. To quantify the cumulative fluid balance over 2 days in relation to body weight, we used the following formula: sum of daily (fluid intake [L] − total output [L]).[24]

Other variables, including comorbidity, laboratory investigations, urine output, need for mechanical ventilation, presence of haemodynamic instability, duration of hospitalisation and causes of mortality, were analysed.

The protocol was interrupted when there was a partial recovery in kidney function (clinical improvement, urine output >2,000 mL/day using furosemide and progressive drop in creatinine (<4 mg/dL and urea <120 mg/dL)), need to change dialysis method because of infectious, mechanical or metabolic complications, more than 28 days of follow-up or death. Mechanical complications were defined as inadequate drainage or dialysate leakage, while infectious complications included exit site infections (purulent drainage from the exit site) or peritonitis, clinically diagnosed in the presence of abdominal pain and cloudy effluent and confirmed by laboratory investigations (total and differential cell counts and effluent culture).[25]

Statistical analysis

Results are presented as mean and standard deviation or median, according to normality characteristics for each variable. Student's *t*-test was used to compare parametric variables, and the Mann–Whitney test was used for non-parametric variables. Categorical variables were expressed as proportions and compared with the chi-square test. Multivariable logistic regression was performed with odds ratio (OR) calculations, including all independent variables that showed association with the mortality, with $p \leq 0.10$, using backward variable selection. Variables not selected by the automated procedure were added back into the models individually to evaluate residual confounding and covariance, and we tested for collinearity among all variables using univariate analysis to identify possible associated confounding variables. All statistical analyses were performed using SPSS 17.0 for Windows statistical software (SPSS, Chicago, Illinois, USA), with a two-sided $p < 0.05$ considered to be statistically significant.

Results

During the study period (10 years), a total of 152 neurocritical AKI patients were treated by AKRT: 38.1% by PD, 58.5% by prolonged HD and 3.3% by CKRT. Among patients treated with PD, the mean age was 61.8 ± 13.2 years, most of patients were male and were in ICU, APACHE II at UCI admission was 16 ± 6; 68.5% needed noradrenaline and 72.4% were on mechanical ventilation. The main neurological diagnoses were intracerebral haemorrhage (31%), stroke (25.9%), subarachnoid haemorrhage (22.4%) and traumatic brain injury (20.7%). The time between the neurocritical event and PD start was 9 ± 3 days. Ischaemic acute tubular necrosis (iATN) was the most common cause of AKI (51.7%), followed by nephrotoxic ATN AKI and septic AKI.

The median number of HVPD sessions was 6.[4–10] Table 1 shows the improvement of metabolic control and fluid balance after PD initiation. Blood urea nitrogen and creatinine levels stabilised after 4 sessions and bicarbonate and pH levels after 3 sessions. The mean UF increased steadily from 1 to 3 sessions and stabilised after 4 sessions at around 2.1 L/day. There was a progressive increase in negative fluid balance from 1 to 3 HVPD sessions, with fluid balance stabilisation after 3 sessions at around −1.3 ± 0.12 L/day. Table 2 shows the prescribed and delivered dialysis dose parameters.

Table 1. Serum BUN, Cr, Bic, pH, K, Na, glucose, osmolality, UF and FB at the beginning of treatment and after each session of peritoneal dialysis in acute-on-chronic liver failure patients.

	Sessions						
	Pré $N = 58$	1 $N = 56$	2 $N = 54$	3 $N = 53$	4 $N = 50$	5 $N = 46$	6 $N = 41$
BUN (mg/dL)	101 ± 31	90 ± 28	78 ± 22	64 ± 19	53 ± 14	48 ± 12	47 ± 10
Cr (mg/dL)	4.2 ± 1.2	4.0 ± 1.4	3.8 ± 0.8	3.4 ± 0.8	2.9 ± 0.9	2.8 ± 0.7	2.7 ± 0.6
Bic (mEq/L)	16.9 ± 3.7	17.5 ± 4.2	21.7 ± 4.2	22.5 ± 3.6	22.6 ± 3.8	23.1 ± 3.4	23.2 ± 3.2
pH	7.23 ± 0.1	7.29 ± 0.1	7.31 ± 0.2	7.32 ± 0.2	7.31 ± 0.2	7.33 ± 0.3	7.34 ± 0.2
K (mEq/L)	5.5 ± 0.8	4.8 ± 0.7	4.3 ± 0.4	4.0 ± 0.3	3.8 ± 0.3	4.0 ± 0.3	3.8 ± 0.2
Na (mEq/L)	144.5 ± 3.51	143 ± 3.22	141.2 ± 2.97	142.1 ± 2.86	143 ± 3.16	141.8 ± 3.23	141.3 ± 2.94
Glucose (mg/dL)	142.8 ± 23.5	166.8 ± 28.5	183.8 ± 33.4	176.3 ± 29.5	163.2 ± 23.9	153.1 ± 21.9	158.8 ± 23.1
Osmolality (osmol/L)	332.2 ± 11.5	328.6 ± 18.5	323.2 ± 13.4	318.3 ± 19.5	314.2 ± 13.9	310.1 ± 11.9	305.8 ± 9.1
UF (L/d)	–	1.1 ± 0.8	1.9 ± 0.9	2.3 ± 0.9	2.1 ± 0.8	2.2 ± 0.7	2.1 ± 0.8
FB (L/day)	4.3 ± 1.1	−0.59 ± 0.4	−1.24 ± 0.9	−1.41 ± 1.7	−1.32 ± 0.8	−1.25 ± 0.7	−1.39 ± 0.7

BUN: blood urea nitrogen; Cr: creatinine; Bic: bicarbonate; K: potassium; Na: sodium; UF: ultrafiltration; FB: fluid balance.

Table 2. Peritoneal dialysis prescription and adequacy.

Variables	
Dialysate volume per cycle (ml)	30 ml/kg (1500–2100 mL)
Inflow time (min)	10
Dwell time (min)	60–90
Outflow time (min)	20
Cycle duration (min)	90–120
Total exchanges per session	12–18
Session duration (h)	24
Total dialysate volume per session (L)	18–36
% glucose	1.5–2.5
Prescribed Kt/V	
Per session	0.4
Weekly	2.8
Delivered Kt/V	
Per session	0.37 ± 0.07[a]
Weekly	2.61 ± 0.34[a]

[a]Without significant difference from prescribed Kt/V.

The delivered urea Kt/V was 0.37 ± 0.09 per session and 2.59 ± 0.31 per week.

Concerning complications related to PD, peritonitis occurred in five patients (8.6%) after 9.1 ± 2.1 PD sessions. Three patients had the catheter removed and the dialysis method changed because of no improvement in laboratory or clinical parameters after 5 days of correct antibiotic treatment. The main etiologic agents were *Pseudomonas aeruginosa* or fungi. Only six patients presented mechanical complications (10.3%), with peri-catheter leakage being the most frequent (66.7%), without need for interruption of therapy. The dialysate volume per cycle was reduced from 30 to 20 mL/kg per cycle (around 1,400 mL/cycle). Two patients had tip catheter migration and the PD needs to be interrupted. Only one patient had wound bleeding. Change in the dialysis modality occurred in five patients: three patients (5.1%) due to refractory peritonitis and two patients (3.5%) due to mechanical complications. Hyperglycaemia occurred in 11 patients (18.9%), and it was corrected using intravenous and intraperitoneal insulin, hypokalaemia in two patients (3.4%) and patients did not present hypo and hypernatraemia. The plasma osmolality ranged from 286 to 291 mOsmol in 24 h during the treatment.

Concerning patient outcomes, 31.1% recovered kidney function, while six patients were kept on dialysis after hospital discharge. In-hospital mortality was 58.6%, and the main cause of death was sepsis (79.46%). Among the survivors, recovery of kidney function (dialysis independence) was 75% at hospital discharge. After 90 days, 22 patients were alive (37.9%) and only 2 were dialysis dependent (3.4%). Figure 1 shows the neurocritical AKI patients outcome treated with PD.

Non-survivors and survivors in-hospital were similar in gender, comorbidities and vasoactive drug use. Azotaemia was the main indication for dialysis in both groups. There was no difference in metabolic control. The groups had similar values of delivered Kt/V per session and weekly (0.38 ± 0.11 vs. 0.37 ± 0.12, p=0.51, and 2.61 ± 0.7 vs. 2.58 ± 0.8, $p = 0.58$) and rate of infectious and mechanical complications related to PD (8.8 vs. 8.33%, $p = 0.92$, and 11.7 vs. 8.3%, $p = 0.57$). There was a difference between the groups in age (63.4 ± 11.7 vs. 57.6 ± 10.6, $p < 0.001$), intracerebral haemorrhage as main neurological diagnoses (44.3 vs. 8.6%, p=0.01), nephrotoxic ATN as the cause of AKI (14.7 vs. 41.7%, $p = 0.04$), mechanical ventilation (88.2 vs. 50%, $p = 0.04$), urine output at day of dialysis indication (378 ± 57 vs. 892 ± 22 mL, $p = 0.04$), fluid overload and UF from the second to the fifth PD sessions (Table 3). Survivors had higher UF and more negative fluid balance than non-survivors. Five factors met the criteria for inclusion in the multivariable analysis: age, nephrotoxic AKI, mechanical ventilation, intracerebral haemorrhage as main neurological diagnoses and fluid overload after two sessions. Intracerebral

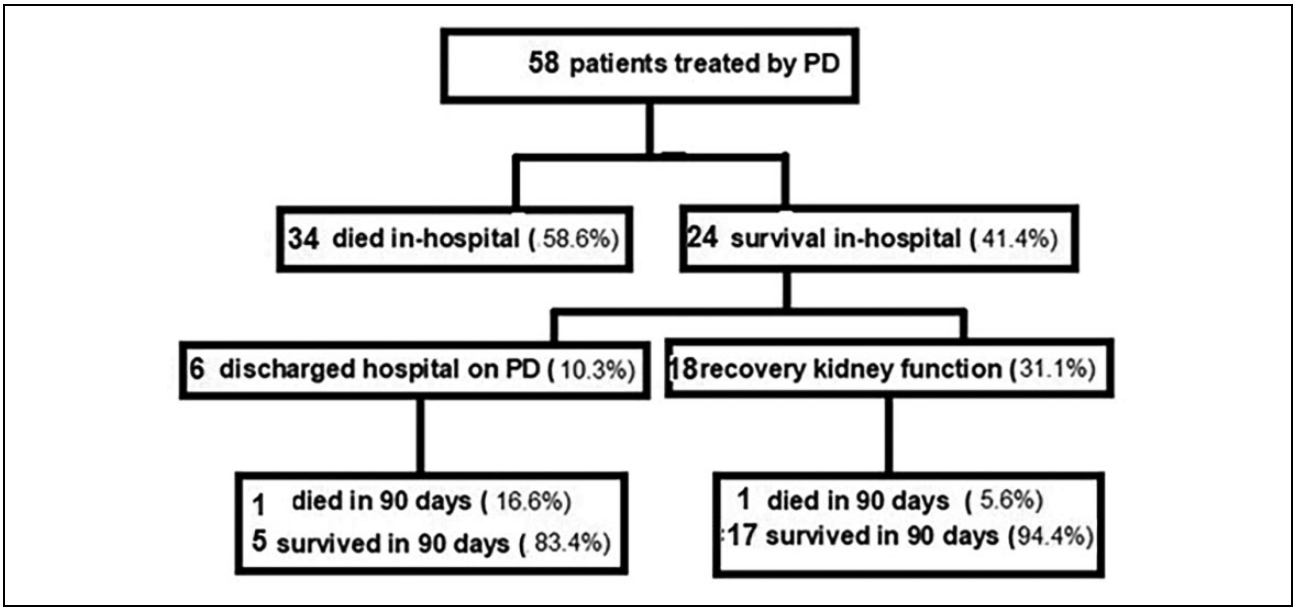

Figure 1. Neurocritical AKI patients outcome treated with peritoneal dialysis.
AKI: acute kidney injury.

Table 3. Neurocritical AKI patients treated with PD according to outcome and main clinical and laboratory characteristics.

	General ($n = 58$)	No-survival ($n = 34$)	Survival ($n = 24$)	p Value
Age (years)	61.8 ± 13.2	63.4 ± 11.7	57.6 ± 10.6	0.001
Male sex (%)	41 (70.6)	24 (70.5)	17 (70.8)	0.97
Weight (kg)	72.6 ± 6.5	73.6 ± 6.1	69.4 ± 6.7	0.08
Diabetes (%)	11 (18.9)	7 (20.5)	4 (16.6)	0.76
Hypertension (%)	15 (25.9)	10 (29.4)	5 (20.8)	0.22
ICU admission (%)	38 (65.5)	28 (84.3).	10 (41.2)	0.03
Noradrenalin use (%)	40 (68.5)	25 (73.5)	15 (62.5)	0.54
Mechanical ventilation (%)	42 (72.4)	30 (88.2)	12 (50)	0.04
Dialysis indication				
Azotemia-uremia (%)	40 (68.5)	25 (73.5)	15 (62.5)	0.54
Hyperkalemia (%)	9 (15.5)	5 (14.7)	4 (16.7)	0.71
Hypervolemia (%)	6 (10.3)	3 (5.2)	3 (12.5)	0.61
Others (%)	3 (5.2)	1 (1.7)	2 (8.3)	0.12
AKI etiology (%)				
Ischaemic AKI	30 (51.7)	28 (73.7)	4 (26.6)	<0.001
Nephrotoxic AKI	15 (25.8)	5 (14.7)	10 (41.7)	0.04
Septic AKI	09 (15.5)	7 (18.4)	3 (20)	0.49
Main neurological diagnosis (%)				
Traumatic brain injury	12 (20.7)	6 (17.6)	6 (25)	0.52
Subarachnoid hemorrhage	13 (22.4)	7 (20.6)	6 (29)	0.93
Stroke	15 (25.9)	7 (20.6)	8 (33.3)	0.28
Intracerebral hemorrhage	18 (31)	15 (44.3)	3 (8.6)	0.01
FO pre dialyis (%)	26 (44.8)	16 (47.1)	10 (41.7)	0.56
Urine output (ml)	582 ± 161	378 ± 57	892 ± 222	0.04
PD complications (%)				
Peritonitis	5 (8.6)	3 (8.8)	2 (8.3)	0.92
Mechanical	6 (10.3)	4 (11.8)	2 (8.3)	0.57
Number of sessions (days)	6 (4–10)	5 (3–9)	7 (4–10)	0.08

(continued)

Table 3. (continued)

	General ($n = 58$)	No-survival ($n = 34$)	Survival ($n = 24$)	p Value
BUN after (mg/dl)				
1st session	91 ± 30	94 ± 32	89 ± 22	0.37
2nd session	84 ± 27	87 ± 31	79 ± 21	0.31
3rd session	70 ± 22	72 ± 27	69 ± 19	0.41
4th session	60 ± 18	61 ± 19	58 ± 17	0.52
5th session	51 ± 12	52 ± 12	49 ± 11	0.71
Creatinine after (mg/dl)				
1st session	4.2 ± 1.5	4.1 ± 1.5	4.4 ± 1.6	0.61
2nd session	4.0 ± 1.3	4.0 ± 1.2	3.9 ± 1.4	0.71
3rd session	3.3 ± 1.4	3.3 ± 1.3	3.4 ± 1.5	0.76
4th session	3.2 ± 1.2	3.2 ± 1.1	3.2 ± 1.3	0.47
5th session	3.0 ± 1.2	3.0 ± 1.1	2.9 ± 1.2	0.21
Bicarbonate after (mEq/L)				
1st session	17.4 ± 4.8	16.4 ± 4.7	18.1 ± 4.9	0.54
2nd session	20.8 ± 4.4	20.1 ± 4.3	21.1 ± 4.7	0.59
3rd session	21.6 ± 3.9	21.2 ± 3.5	21.9 ± 4.5	0.69
4th session	22.6 ± 3.8	22.5 ± 3.4	22.8 ± 4.4	0.71
5th session	23.2 ± 3.6	22.8 ± 3.1	23.7 ± 4.1	0.77
UF after (l)				
1st session	0.97 (−0.63–1.5)	0.83 (−0.33–1.5)	1.3 (−0.8−1.5)	0.14
2nd session	2.1 (0.9−3.1)	1.9 (0.9−2.8)	2.4 (0.9−3.3)	0.05
3rd session	1.8 (0.9−2.9)	1.5 (0.8−2.3)	2.5 (1.0−3.7)	0.04
4th session	1.9 (0.9−3.1)	1.5 (0.8−2.4)	2.2 (1.4−3.4)	0.04
5th session	1.8 (1.1−2.6)	1.4 (0.9−1.6)	2.0 (1.9−3.3)	0.04
FB after (l)				
1st session	1.12 ± 0.3	1.22 ± 0.4	0.8 ± 0.1	0.37
2nd session	−1.25 ± 0.6	−1.09 ± 0.4	−1.88 ± 0.7	0.04
3rd session	−1.66 ± 0.2	−1.06 ± 0.2	−1.95 ± 0.3	0.03
4th session	−1.55 ± 0.6	−1.15 ± 0.4	−1.79 ± 1.1	0.04
5th session	−1.61 ± 0.8	−1.01 ± 0.8	−1.82 ± 0.9	0.06
Delivered Kt/V				
Per session	0.38 ± 0.12	0.38 ± 0.11	0.37 ± 0.12	0.51
Weekly	2.60 ± 0.7	2.61 ± 0.7	2.58 ± 0.8	0.58

AKI: acute kidney injury; FO: fluid overload; FB: fluid balance; HRS: hepatorenal syndrome; MELD: model of end-stage liver disease.

haemorrhage as main neurological diagnoses (OR = 1.15, 95% confidence interval (CI) = 1.09–2.11, $p = 0.03$), nephrotoxic AKI (OR = 0.78, 95% CI = 0.69–0.95, $p = 0.03$), mechanical ventilation (OR = 1.54, 95% CI = 1.17–2.46, $p = 0.01$) and negative fluid balance after two PD sessions (OR = 0.94, 95% CI = 0.74–0.97, $p = 0.009$) were associated significantly with death, as shown in Table 4.

Table 4. Association (with $p < 0.25$) between multiple adjusted patient and peritoneal dialysis characteristics and death.

Variables	OR (95% CI)	p Value
Age (per 1 year)	1.02 (0.98–1.06)	0.18
Nephrotoxic ATN	0.78 (0.69–0.95)	0.03
Mechanical ventilation	1.54 (1.17–2.46)	0.01
Intracerebral haemorrhage	1.15 (1.09–1.1)	0.03
FB (per −0.1 L/day)	0.94 (0.74–0.97)	0.009

OR: odds ratio; CI: confidence interval; ATN: acute tubular necrosis; FB fluid balance (from 2nd to 4th peritoneal dialysis session); FB: fluid balance (L/day after the second HVPD session); HVPD: high-volume peritoneal dialysis.

Discussion

The interest in PD for treating AKI patients has increased, and PD is currently used in low- and middle-income countries because of its lower cost and minimal infrastructural requirements. Studies from these countries have shown that, with careful thought and planning, critically ill patients can be successfully treated using PD, achieving adequate metabolic and fluid control and a mortality rate around 50%.[19–24] Recently, the pandemic of SARS-CoV-2 infection has overwhelmed HD capacity worldwide, and acute PD has been an excellent alternative in developed countries as well.[26,27] In this study, we evaluated the role of PD in treating neurocritical patients with AKI.

In neurocritical patients, abrupt changes in osmolality and volemia as well as anticoagulation risk can alter cerebral blood flow, cerebral perfusion pressure and on the whole modifying ICP.[1] Some therapies, including PD, can decrease this risk.[1,2,28,29]

Our study showed encouraging results for BUN, creatinine, bicarbonate, sodium, potassium and pH levels. Metabolic and fluid control were achieved after 3 or 4 PD sessions using HVPD and prescribed Kt/V of 0.4. The delivered weekly Kt/V was around 2.59, and one session lasted for 24 h. Mean UF increased steadily from 1 to 3 sessions and stabilised after 4 sessions at around 2.1 L/day, and there was a progressive increase in negative fluid balance from 1 to 3 HVPD sessions, with fluid balance stabilisation after 3 sessions at around -1.3 ± 0.12 L/day. However, there is objective evidence that the lower target (achieved weekly Kt/V around 2.2) and recommended dwell times published in the ISPD guidelines (between 90 min and 120 min) are sufficient for treating AKI with PD and do not lead to inferior outcomes.[30] Another question worthraising are concerns regarding the importance of measuring urea clearances. The Kt/V urea may serve as a marker for other small solute clearances, as mentioned above, which may be important in the initial phases of treatment but may not be as relevant for metabolic control (BUN and K levels) and for medium-term outcomes, suggesting that a lower dialysis dose threshold may be permissible.[31]

Concerning metabolic complications, hyperglycaemia occurred in less than 20% of patients and it was corrected in 2 days using intravenous and intraperitoneal insulin, patients did not present hypo and hypernatraemia and plasma osmolality ranged less than 6 osmol/L in 24 h during the treatment. There are few reports on this group of patients, and its inappropriate use could increase cerebral oedema, as occurs with other AKRT methods.[31] Furthermore, case series on PD have showed that changes in ICP are less than with HD (with cerebral perfusion pressure even improving in some cases) and without the complications of anticoagulation.[32–35]

A controlled correction of serum sodium is essential in neurocritical care patients. Despite the fact that PD solutions contain an Na^+ level of 132 mEq/L, this concentration decreases in the first phases of dwell time until the first or second hour, a phenomenon known as 'sodium sieving' and thus may be beneficial for maintaining an optimal serum sodium.[36–38] An increase in natraemia has been reported in the first five sessions of the HVPD method when using a solution with 132 mEq/L of sodium; a natraemia of around 142 mEq/L is maintained in later sessions.[16]

Peritonitis occurred in 8.6%, and it was similar to that reported in the literature (10.3–12.3%). According to literature, the incidence of peritonitis has been reduced, and the risk was similar to using other forms of extracorporeal therapies for AKI due to better PD catheter implantation techniques, the use of cyclers and flexible catheters.[17,39,40] Al-Hwiesh reported that infectious complications were significantly less common with TPD compared with CVVHDF (9.5 vs. 17.7%), proposing that repeated catheterisation and manipulation by different operators are avoided with PD.[12] Most of the patients with peritonitis had the catheter removed and the dialysis method changed because of lack of success with the treatment.

Only 10.3% of patients presented mechanical complications and peri-catheter leakage was the most frequent (66.7%), although it did not lead to interruption of therapy. The dialysate volume per cycle was reduced from 30 to 20 ml/kg per cycle, and PD treatment was performed successfully. Change in the dialysis method occurred only in five patients due to refractory peritonitis (three patients) and due to mechanical complications (two patients).

Concerning patient outcomes, among the survivors, recovery of kidney function (dialysis independence) was 75% at hospital discharge. After 90 days, 37.9% of patients were alive, and only 3.4% were dialysis dependent. We observed a mortality rate around 58%, within the range of survival reported by other studies on patients with AKI who require AKRT.[5] Intracerebral haemorrhage as main neurological diagnosis, need for mechanical ventilation and fluid balance after two PD sessions were associated with death. Unfortunately, there are no data on neurocritical care residual or functional status of these patients.

Our results agree with previous studies, including systematic reviews, which have shown that fluid overload is a risk factor and predictor of death in critical patients.[41–44] In our study, negative fluid balance was associated with lower mortality. Previous studies reported similar results. In a European multi-centre trial, Payen et al.[43] observed positive fluid balance as a risk factor for mortality in 60 days in critical AKI patients. Zhang et al.[42] in a multi-centre ICU study showed the fluid balance was greater in patients with AKI than in patients without AKI and that a higher cumulative fluid balance was an important factor associated with 28-day mortality following AKI. A retrospective analysis of postoperative percentage fluid overload in patients at AKI stage 3 after cardiac surgery showed that fluid overload >7.2% was significantly associated with reduced 90-day survival.[44] In neurological patients, the association between negative fluid balance and reduction of cerebral oedema can add explanation in the understanding of the positive fluid balance be identified as risk factor for mortality. Furthermore, the fluid overload can also indicate endothelial dysfunction and disease severity fluid, contributing to the higher mortality.

Regarding ICH, patients survival remains compromised despite the advances in the management of this pathology. The acute deterioration of kidney function and the intensive blood pressure control may increase the risk of death.[45,46] Nevertheless, PD could be an option in ICH patients because therapies such as prolonged HD report an increase in perihematomal oedema and worsening clinical outcomes.[47] Therefore, further studies must be carried out in this group of patients to define more optimal therapies and the role of PD compared to IHD or CKRT.

In this study, both the in-hospital mortality rate and recovery of kidney function were similar to those found in previous studies that used PD for treating AKI patients, such as type 1 cardio-renal syndrome and septic patients,[19,20–23,48] and better than other studies that treated cirrhotic patients by PD.[49]

The choice of the AKRT in neurocritical patients is difficult to make. The most important limiting factors of intermittent therapies are abrupt changes in osmolality and volemia secondary to effective therapy. Hypotension decreases the effectiveness of AKRT and aggravates ischemic injury, delaying the recovery of kidney and brain function. When compared to intermittent therapies, continuous methods offer greater haemodynamic stability and are often preferred for patients with arterial hypotension.[50–52] Regarding the mode of dialysis, CKRT does not improve mortality in comparison with intermittent HD; however, CKRT may be well-tolerated in patients with unstable conditions, including intracranial hypertension.[50–52]

In this scenario, PD may be better tolerated by neurocritical patients than intermittent or prolonged HD, with no increase in the number of complications, enabling removal of solutes such as ammonia, urea and fluid and not exposing patients to anticoagulants and large variations in sodium and osmolality.

To the best our knowledge, this study is unique in providing detailed insights into PD treatment for neurocritical patients and identifying risk factors for death. Some limitations of this study must be considered. Firstly, the study was performed in a single centre, and the number of patients was small. Secondly, it was an observational study, and PD treatment was not compared with another dialysis modality. Thirdly, there are no data on neurocritical care residual or functional status of these patients. In fourth place, the initiation of dialysis occurred so long after the neurological event, and it is unlikely that the modality of dialysis at this point would have had much influence on intracerebral pressures or haemodynamics. Finally, there are many factors that affect the prognosis of patients with neurocritical patients, for example, fluid overload, and we need to perform a propensity analysis to further explore this issue.

In conclusion, the findings of our study suggest that with careful thought and planning, neurological patients can be successfully treated using PD, which may provide adequate treatment for most neurocritical patients without contraindications for PD use, allowing adequate metabolic and fluid control, with no increase in the number of infectious, metabolic or mechanical complications. Mechanical ventilation and intracerebral haemorrhage were factors associated with mortality, while nephrotoxic AKI and negative fluid balance were protective factors. Further studies are needed to investigate better the role of PD in neurocritical patients with AKI, comparing it with other HD modalities in the treatment for these patients.

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Author contributions

DP and ALB made substantial contributions to conception and design, acquisition of data, and analysis and interpretation of data and were involved in drafting the manuscript. GRG revising it critically for important intellectual content. DP gave final approval of the version to be published. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Declaration of conflicting interests

The authors declared the following potential conflicts of interest with respect to the research, authorship and/or publication of this article: The authors report no conflicts of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article. The authors alone are responsible for the content and writing of this article. The lead authors (DP and ALB) confirm that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as originally planned (and, if relevant, registered) have been explained.

Ethical approval

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