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PERSPECTIVE

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How I prescribe prolonged intermittent renal replacement therapy

Edward G. Clark^{1*} and Anitha Vijayan²

Abstract

Prolonged Intermittent Renal Replacement Therapy (PIRRT) is the term used to define 'hybrid' forms of renal replacement therapy. PIRRT can be provided using an intermittent hemodialysis machine or a continuous renal replacement therapy (CRRT) machine. Treatments are provided for a longer duration than typical intermittent hemodialysis treatments (6–12 h vs. 3–4 h, respectively) but not 24 h per day as is done for continuous renal replacement therapy (CRRT). Usually, PIRRT treatments are provided 4 to 7 times per week. PIRRT is a cost-effective and flexible modality with which to safely provide RRT for critically ill patients. We present a brief review on the use of PIRRT in the ICU with a focus on how we prescribe it in that setting.

Introduction

Prolonged Intermittent Renal Replacement Therapy (PIRRT) is the term that broadly encompasses 'hybrid' forms of renal replacement therapy (RRT). PIRRT treatments are provided for a longer duration than are intermittent hemodialysis (IHD) treatments (6–12 h vs. 3–4 h, respectively) but not 24 h per day as is done for continuous renal replacement therapy (CRRT). PIRRT is typically provided 4 to 7 times per week [1].

While PIRRT is less commonly used in ICUs than IHD or CRRT, its use has been progressively increasing in low- and middle-income countries [2, 3] since its initial descriptions in the literature in the late 1990s [4, 5]. Its routine use in some high-income countries (e.g., institutions in New Zealand [6] and Canada [7]) is also long-established. It is a cost-effective (as compared to CRRT [7, 8]) and flexible modality with which to safely provide RRT for hemodynamically unstable patients. During the

COVID-19 pandemic, PIRRT was rapidly adopted at some institutions to maximize their acute RRT capacity during surge. [9–11].

Indications for PIRRT

KDIGO 2012 guidelines state that CRRT is the treatment of choice for hemodynamically unstable patients, including those on extracorporeal support such as ECMO. However, at that time data on PIRRT were scarce. At present, PIRRT is used as a substitute for CRRT to treat hemodynamically unstable patients with acute kidney injury (AKI) or ESRD [12]; it can also be used in patients during de-escalation of treatment in the ICU [13], or as a substitute for IHD. Less well-studied than IHD or CRRT, there is no evidence suggesting significant differences in mortality or kidney recovery with the use of PIRRT to manage severe AKI in critically ill patients as compared to CRRT [14]. Reducing the efficiency of solute clearance (thereby reducing osmotic shifts) and extending the duration of treatment (thereby lowering the ultrafiltration rate) make PIRRT less likely to provoke hemodynamic instability during RRT (HIRRT) relative to IHD [15]. As an intermittent therapy, PIRRT facilitates the performance of diagnostic imaging, rehabilitation, and other procedures, and can often be provided overnight.

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In certain situations, PIRRT is relatively contraindicated. For patients with intoxications or extreme electrolyte disturbances where highly efficient small molecule clearance is desired, IHD should be favored over PIRRT (or CRRT). Conversely, in patients with traumatic brain injury, increased intracranial pressure or severe hyponatremia, CRRT should be favored over PIRRT (or IHD).

PIRRT modalities

PIRRT can be delivered using a standard IHD machine (with a connection to a central purified water-supply or the use of a portable/built-in reverse-osmosis machine) or a CRRT machine using standard commercially available CRRT solutions. In either case, adjustments are made to the blood flow rate (Q_b), and dialyzer rate (Q_d) and/or replacement fluid rates. These modifications are made to reduce the efficiency of solute clearance relative to standard IHD (and provide it for a longer duration) or increase clearance relative to CRRT (and provide it for a shorter duration). When using a conventional IHD machine to provide PIRRT, the machine software may not allow the Q_d to be reduced enough to markedly decrease the efficiency of solute clearance. In such cases, a CRRT or pediatric IHD dialyzer (filter) with a relatively small surface area may be utilized to further reduce efficiency. Depending on the machines used and local experience, specific PIRRT modalities utilize diffusive clearance (i.e., hemodialysis; e.g., sustained low-efficiency (daily) dialysis [SLED/SLEDD]), convective clearance (i.e., hemofiltration; e.g., accelerated veno-venous hemofiltration [AVVH]) or both (i.e., hemodiafiltration; e.g., sustained low-efficiency (daily) diafiltration [SLED-f/SLEDD-f]).

Vascular access

Vascular access considerations for patients with AKI are similar to when prescribing CRRT [16]. For patients with pre-existing kidney failure and an arteriovenous fistula (AVF) or arteriovenous graft (AVG), unless IHD-trained nurses are routinely involved in the provision of PIRRT and measures are in-place to prevent dislodgement of access needles, a hemodialysis catheter is required for PIRRT.

Anticoagulation

There is less need for anticoagulation with the use of PIRRT compared with CRRT, largely due to the higher Q_b . In the absence of another indication for anticoagulation, we prescribe PIRRT without any anticoagulation (i.e., saline flushes only). When anticoagulation is indicated due to issues with filter clotting or otherwise,

unfractionated heparin is most commonly used. If CRRT machines are used to provide PIRRT and regional citrate anticoagulation is possible, it is the option of choice.

Typical treatment parameters for PIRRT

Table 1 details sample PIRRT prescriptions according to whether a conventional IHD machine or a CRRT machine is being used and relative to standard IHD and CRRT treatments. Successful development and implementation of routine PIRRT protocols necessitate a collaborative approach. The input of nephrologists, critical care physicians, nurses, pharmacists and administrators is required.

Complications/safety

When ordering PIRRT that is delivered using a conventional IHD machine, use of a low dialyzer temperature (i.e., 35–35.5 °C) [17], relatively high dialyzer sodium and calcium concentrations (e.g., 145 mmol/L and 1.5 mmol/L, respectively) may help mitigate HIRRT [18]. In patients with significant hyponatremia (e.g., serum sodium \leq 130 mmol/L), the dialyzer sodium should be reduced to a level that will prevent overly rapid correction assuming that equilibration between the serum and dialyzer sodium will occur before the end of treatment. When using a conventional IHD machine with on-line generation of dialyzer, dialyzer bicarbonate levels must also be reduced to allow for generation of dialyzer sodium concentrations at the lower end of what the machine allows (typically \sim 130 mmol/L). Similarly, when ordering dialyzer potassium concentration, it is safest to assume that complete equilibration will occur prior to the end of the treatment. Thus, unless the patient is profoundly hyperkalemic and/or more-rapid correction is mandated (i.e., serum potassium \geq 6.5 mmol/L or acutely rising) then a dialyzer potassium of 4 mmol/L can be used routinely to avoid precipitating hypokalemia.

Hypophosphatemia is a frequent complication of any continuous or prolonged RRT and is often under recognized [19]. Hypophosphatemia during RRT can lead to tissue hypoxia [20] and is associated with prolonged ventilator dependence [21]. Pre-emptive management is key since effects of phosphate depletion can occur even without overt hypophosphatemia. At one author's (AV) institution, the PIRRT protocol calls for starting oral supplementation when serum phosphate is less than 1.1 mmol/L. At the other author's (EC) institution, where IHD equipment is used to provide PIRRT, a phosphate additive is routinely added to dialyzer when serum

phosphate is less than 1.6 mmol/L. Other pre-emptive strategies include using phosphate-containing solutions (if CRRT equipment is used to provide PIRRT). Intravenous phosphate supplementation may be required for moderate to severe hypophosphatemia (<0.6 mmol/L).

Antibiotic and other medication dosing data in PIRRT are limited and, ideally, should be considered in conjunction with the input of a critical care or nephrology pharmacist. For medications cleared during RRT, augmented or additional dosing may be required. For example, intravenous vancomycin may need to be given immediately before and after a 10–12 h PIRRT session to ensure an adequate therapeutic level during and post-treatment. Table 2 provides additional details regarding dosing of selected antibiotics in patients receiving PIRRT [22–28], a topic that has been explored in greater detail by other reviews [29, 30].

Dose/adequacy

Unlike dosing recommendations for CRRT and IHD (based on RENAL [31] and ATN [32] trials), there is no standard recommendation for dosing of PIRRT. Despite significant pitfalls in its use, urea kinetics remain the

mainstay of determining adequacy of clearance during RRT, even in AKI. When prescribing PIRRT as a substitute for CRRT, a minimum weekly standard Kt/Vurea of 6 may be required. If using as a substitute for IHD or as a transition therapy, then lower flow rates or decreased frequency of treatments may suffice, as weekly standard Kt/Vurea recommendations for IHD is 2 [1]. It should be noted that volume overload is also an indication for RRT and frequency of PIRRT treatments ultimately will also depend on volume status and metabolic derangements such as hyperkalemia.

Conclusions

The various forms of PIRRT used in ICU allow for cost-effective and flexible treatments for critically ill patients with kidney failure. As detailed in Table 1, practical considerations related to its application depend on whether IHD or CRRT machines are used to provide PIRRT. As is the case for our colleagues who prescribe CRRT [16], at institutions that provide PIRRT, we similarly advocate for its protocolized application accompanied by routine monitoring of quality and safety.

Table 1 PIRRT Using IHD and CRRT Machines in Comparison with Standard IHD and CRRT Prescriptions

Parameter	Modality			Standard CRRT
	Standard Intermittent IHD	PIRRT		
		Using IHD Machine	Using CRRT Machine	
Clearance mode	Diffusion	Diffusion or Diffusion + Convection	Diffusion or Convection or Diffusion + Convection	
Blood flow rate	≥ 300 mL/min	100–300 mL/min		100–200 mL/min
Duration	3–4 h	6–12 h	8–12 h	Continuous
Frequency	3–4 days/week	4–7 days/week		
Dialyrate rate	500–800 mL/min	100–400 mL/min		10–30 mL/min
Replacement Rate*	N/A	1–2 L/hour	20–40 mL/min	10–30 mL/min
Dialyzer Surface area	1.0–2.5 m ²	0.6–2.5 m ²	0.6–1.5 m ²	
Need for Anticoagulation	+	+		+++
Dialyrate [Na ⁺]	145 mmol/L ^δ		140 mmol/L ^ψ	
Dialyrate [K ⁺]	4 mmol/L ^δ			
Dialyrate [Ca ++]	1.5 mmol/L ^δ		1.75 mmol/L (0 mmol/L if using RCA) ^ψ	
Dialyrate [HCO ₃]	24–36 mmol/L ^δ		32 mmol/L ^ψ	
Options for pre-emptive PO ₄ supplementation once serum [PO ₄] ≤ 1–1.6 mmol/L	Add PO ₄ to dialyrate Oral/enteral PO ₄ administration		Add PO ₄ to standard CRRT fluids or switch to commercially available PO ₄ -containing fluids	

* Only applicable if convective clearance (hemofiltration) is being employed

^δ Standard concentrations; may be adjusted as indicated clinically

^ψ Using commercially available solutions

[Na⁺], sodium concentration; [K⁺], potassium concentration; [Ca ++], calcium concentration; [HCO₃], bicarbonate solution; RCA, regional citrate anticoagulation; [PO₄], phosphate concentration

Table 2 Prescription of Selected Anti-infective Agents for Critically Ill Patients Receiving PIRRT

Anti-infective Agent [Relevant REFs]	Suggested Dosing Regimen*	Comments
Vancomycin [22, 23] Piperacillin [24, 25]	Loading dose of 2400 mg then 1600 mg post-treatment 3 g every 8 h for susceptible organisms with MIC ≤ 16 mg/L OR 9 g dose as a continuous infusion every 24 h for susceptible organisms with MIC ≤ 32 mg/L	Clearance with PIRRT is ~ 3X higher than is described for CRRT
Meropenem [23, 25–27]	Maintenance dose of 1 g every 8 h or every 12 h	Wide variation across institutions; most frequently recommended regimen: 1 g every 12 h [26]
Fluconazole [28]	Loading dose of 800 mg followed by 400 mg twice daily (q12h or pre- and post- PIRRT)	Recommendation based on Monte Carlo simulations using a pharmacokinetic model of PIRRT. Directly measured pharmacokinetic data for fluconazole (and most anti-infective agents) are limited in this setting

REFs, references; MIC, minimum inhibitory concentration; PIRRT, prolonged intermittent renal replacement therapy; CRRT, continuous renal replacement therapy

*Suggested dosing is based on an assumption that PIRRT is provided as sustained low-efficiency dialysis using a dialyzer with a surface area of 0.7 m², Blood Flow Rate (Qb) of 200 ml/min, Dialyzer Flow Rate (Qd) of 300 ml/min and prescribed as 8-h sessions once daily. Dosing regimens should be adjusted according to the relative efficiency/clearance mode(s) of PIRRT being provided, residual kidney function and other standard dosing considerations (e.g., patient weight, volume of distribution, etc.). A more detailed summary of anti-infective dosing studies across various forms of PIRRT can be found in other reviews [29, 30]. We suggest that all anti-infective agents for critically ill patients receiving PIRRT are prescribed in conjunction with a critical care pharmacist and guided by directly measured levels, whenever possible

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Not applicable.

Competing interests

E.G. Clark reports being on the editorial board of the Canadian Journal of Kidney Health and Disease. A. Vijayan reports consultancy for Astute and NxStage; ownership interest in Outset (stock only); research funding from Astellas and Spectral; honoraria from NxStage; an advisory or leadership role for NxStage; and being a member of the National Kidney Foundation.

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References:

- Levine Z, Vijayan A. Prolonged intermittent kidney replacement therapy. *Clin J Am Soc Nephrol*. CJASN 2022.
- Bouchard J, Acharya A, Cerda J, Maccariello ER, Madarasu RC, Tolwani AJ, Liang X, Fu P, Liu ZH, Mehta RL. A Prospective international multicenter study of AKI in the intensive care unit. *Clin J Am Soc Nephrol* CJASN. 2015;10(8):1324–31.
- Vangala C, Shah M, Dave NN, Attar LA, Navaneethan SD, Ramanathan V, Crowley S, Winkelmayer WC. The landscape of renal replacement therapy in Veterans Affairs Medical Center intensive care units. *Ren Fail*. 2021;43(1):1146–54.
- Kumar VA, Craig M, Depner TA, Yeun JY. Extended daily dialysis: a new approach to renal replacement for acute renal failure in the intensive care unit. *Am J Kidney Dis*. 2000;36(2):294–300.
- Schlaepfer C, Amerling R, Manns M, Levin NW. High clearance continuous renal replacement therapy with a modified dialysis machine. *Kidney Int Suppl*. 1999;72:S20–23.
- Marshall MR, Creamer JM, Foster M, Ma TM, Mann SL, Fiaccadori E, Maggiore U, Richards B, Wilson VL, Williams AB, et al. Mortality rate comparison after switching from continuous to prolonged intermittent renal replacement for acute kidney injury in three intensive care units from different countries. *Nephrol Dial Trans Off Publ European Dial Trans Assoc European Renal Assoc*. 2011;26(7):2169–75.
- Berbec AN, Richardson RM. Sustained low-efficiency dialysis in the ICU: cost, anticoagulation, and solute removal. *Kidney Int*. 2006;70(5):963–8.
- Schwenger V, Weigand MA, Hoffmann O, Dikow R, Kihm LP, Seckinger J, Miftari N, Schaefer M, Hofer S, Haar C, et al. Sustained low efficiency dialysis using a single-pass batch system in acute kidney injury - a randomized interventional trial: the ReNal replacement therapy study in intensive care unit PatiEnts. *Crit Care*. 2012;16(4):R140.
- Goldfarb DS, Benstein JA, Zhdanova O, Hammer E, Block CA, Caplin NJ, Thompson N, Charytan DM. Impending shortages of kidney replacement therapy for COVID-19 patients. *Clin J Am Soc Nephrol* CJASN. 2020;15(6):880–2.
- Burgner A, Golper T. Walkaway PIRRT (as SLED) for acute kidney injury. *Clin J Am Soc Nephrol* CJASN. 2020;16(1):138–40.
- Yessayan LT, Heung M, Girard FA, Shaikhouni S, Szamosfalvi B. Deployment of a new CRRT/PIRRT device during the COVID-19 pandemic emergency: organizational challenges and implementation results. *Blood Purif*. 2021;50(3):390–8.
- Palevsky PM, Liu KD, Brophy PD, Chawla LS, Parikh CR, Thakar CV, Tolwani AJ, Waikar SS, Weisbord SD. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis*. 2013;61(5):649–72.
- Allegretti AS, Endres P, Parris T, Zhao S, May M, Sylvia-Reardon M, Bezreh N, Culbert-Costley R, Ananian L, Roberts RJ, et al. Accelerated venovenous hemofiltration as a transitional renal replacement therapy in the intensive care unit. *Am J Nephrol*. 2020;51(4):318–26.
- Ye Z, Wang Y, Ge L, Guyatt GH, Collister D, Alhazzani W, Bagshaw SM, Belle-Cote EP, Fang F, Hou L, et al. Comparing renal replacement therapy modalities in critically ill patients with acute kidney injury: a systematic review and network meta-analysis. *Crit Care Explor*. 2021;3(5): e0399.
- Douvrin A, Zeid K, Hiremath S, Bagshaw SM, Wald R, Beaubien-Souligny W, Kong J, Ronco C, Clark EG. Mechanisms for hemodynamic instability related to renal replacement therapy: a narrative review. *Intensive Care Med*. 2019;45(10):1333–46.
- See EJ, Bellomo R. How I prescribe continuous renal replacement therapy. *Crit Care*. 2019;25(1):1.
- Edrees FY, Katari S, Baty JD, Vijayan A. A pilot study evaluating the effect of cooler dialysate temperature on hemodynamic stability during prolonged intermittent renal replacement therapy in acute kidney injury. *Crit Care Med*. 2019;47(2):e74–80.
- Douvrin A, Malhi G, Hiremath S, McIntyre L, Silver SA, Bagshaw SM, Wald R, Ronco C, Sikora L, Weber C, et al. Interventions to prevent hemodynamic instability during renal replacement therapy in critically ill patients: a systematic review. *Crit Care*. 2018;22(1):41.
- Pistolessi V, Zeppilli L, Fiaccadori E, Regolisti G, Tritapepe L, Morabito S. Hypophosphatemia in critically ill patients with acute kidney injury on renal replacement therapies. *J Nephrol*. 2019;32(6):895–908.
- Sharma S, Brugnara C, Betensky RA, Waikar SS. Reductions in red blood cell 2,3-diphosphoglycerate concentration during continuous renal replacement therapy. *Clin J Am Soc Nephrol* CJASN. 2015;10(1):74–9.
- Sharma S, Kelly YP, Palevsky PM, Waikar SS. Intensity of renal replacement therapy and duration of mechanical ventilation: secondary analysis of the acute renal failure trial network study. *Chest*. 2020;158(4):1473–81.
- Kanji S, Roberts JA, Xie J, Zelenitsky S, Hiremath S, Zhang G, Watpool I, Porteous R, Patel R. Vancomycin population pharmacokinetics in critically ill adults during sustained low-efficiency dialysis. *Clin Pharmacokinet*. 2020;59(3):327–34.
- Oliveira MS, Machado AS, Mendes ET, Chaves L, Perdigao Neto LV, Vieira da Silva Jr C, Cavani Jorge Santos SR, Sanches C, Macedo E, Levin AS. Pharmacokinetic and pharmacodynamic characteristics of vancomycin and meropenem in critically ill patients receiving sustained low-efficiency dialysis. *Clin Ther*. 2020;42(4):625–33.
- Kanji S, Roberts JA, Xie J, Alobaid A, Zelenitsky S, Hiremath S, Zhang G, Watpool I, Porteous R, Patel R. Piperacillin Population pharmacokinetics in critically ill adults during sustained low-efficiency dialysis. *Ann Pharmacother*. 2018;52(10):965–73.
- Liebchen U, Paal M, Bucher V, Vogeser M, Irlbeck M, Schroeder I, Zoller M, Scharf C. Trough concentrations of meropenem and piperacillin during slow extended dialysis in critically ill patients with intermittent and continuous infusion: a prospective observational study. *J Crit Care*. 2022;67:26–32.
- Mei JP, Ali-Moghaddam A, Mueller BA. Survey of pharmacists' antibiotic dosing recommendations for sustained low-efficiency dialysis. *Int J Clin Pharm*. 2016;38(1):127–34.
- Lewis SJ, Kays MB, Mueller BA. Use of monte carlo simulations to determine optimal carbapenem dosing in critically ill patients receiving prolonged intermittent renal replacement therapy. *J Clin Pharmacol*. 2016;56(10):1277–87.
- Gharibian KN, Mueller BA. Fluconazole dosing predictions in critically-ill patients receiving prolonged intermittent renal replacement therapy: a Monte Carlo simulation approach. *Clin Nephrol*. 2016;86(7):43–50.
- Brown P, Battistella M. Principles of Drug Dosing in Sustained Low Efficiency Dialysis (SLED) and Review of Antimicrobial Dosing Literature. *Pharmacy* 2020, 8(1).
- Sethi SK, Krishnappa V, Nangethu N, Nemer P, Frazee LA, Raina R. Antibiotic dosing in sustained low-efficiency dialysis in critically ill patients. *Can J Kidney Health Dis*. 2018;5:2054358118792229.
- Investigators RRTS, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, Lo S, McArthur C, McGuinness S, Myburgh J, et al. Intensity of continuous renal-replacement therapy in critically ill patients. *N Engl J Med*. 2009;361(17):1627–38.

32. Network VNA-RFT, Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, Finkel K, Kellum JA, Paganini E et al. Intensity of renal support in critically ill patients with acute kidney injury. *New England J Med* 2008, 359(1):7–20.

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