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ISPD guidelines for peritoneal dialysis in acute kidney injury: 2020 update (adults)

ABSTRACT

The use of peritoneal dialysis (PD) to treat patients with acute kidney injury (AKI) has become more popular among clinicians following evidence that its efficacy is similar to/comparable to other extracorporeal therapies. Although it has been extensively used in low-resource environments for many years, there is now a renewed interest in the use of PD to manage patients with AKI (including patients in intensive care units) in higher-income countries. Here we present the update of the International Society for Peritoneal Dialysis guidelines for the use of PD in AKI. These guidelines extensively review the available literature and present updated recommendations regarding peritoneal access, dialysis solutions, and the prescription of dialysis with revised targets of solute clearance.

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Key words: AKI, critical care, CRRT, dialysis, guidelines, intensive care, sepsis

INTRODUCTION

Peritoneal dialysis (PD) has been effectively used to treat acute kidney injury (AKI) since 1946 [1]. Initial problems relating to access, overhydration, and hyperchloremic acidosis were overcome and with improved outcomes, PD became a well-respected dialysis modality for AKI [2, 3]. The introduction of extracorporeal continuous renal replacement therapy (CRRT) in intensive care units (ICUs) led to a rapid decline in the use of PD despite no evidence of the superiority of this modality in terms of outcomes, even when compared with intermittent hemodialysis (IHD) [3–5]. Despite this decline in the use of PD, many clinicians feel that acute PD is still a suitable modality for treating patients with AKI, both in the intensive care and in the ward environment [6]. Recent studies have demonstrated that there is equivalent survival (and perhaps a shorter need for renal replacement therapy [RRT]) using PD compared with other extracorporeal modalities, and as a result, there has been renewed interest in the use of PD for AKI [7, 8]. Acute PD is largely practiced in Low/Low Middle-Income Countries (LLMICs) due to several significant advantages over CRRT/IHD: the lack of requirements for water and electricity, significantly less training for nursing staff, cardiovascular stability in hypotensive patients, and most significantly — costs [9, 10]. These benefits and the simplicity of acute PD are the reason why the Saving Young Lives (SYL) program established by the International Society of Nephrology has dedicated its efforts to developing acute PD programs in these countries. Thus far over 500 patients in SYL centers have been treated with a > 60% survival along with recovery of renal function [11–15]. Finally, the recent Covid-19 pandemic has highlighted the benefits of acute PD in patients who have a hypercoagulable state, especially when extracorporeal therapy options are limited due to demands on machines, supplies, and staffing [16].

These guidelines have been developed under the auspices of the International Society for Peritoneal Dialysis (ISPD) as an update to the previous guidelines published in 2014 [17, 18]. The new guidelines have been developed for practitioners working in very different clinical and institutional conditions, including the different availability of dialysis equipment. Therefore, based on the available data and the opinion of the authors, 'minimum standard' or 'optimal' management standards have been formulated to ensure that treatment benefits will outweigh potential risks.

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RECOMMENDATION 1: IS PD A SUITABLE MODALITY FOR TREATING AKI?

PD should be considered a suitable modality for the treatment of AKI in all settings **(1B)**.

There are several advantages of PD over extracorporeal therapy in the treatment of AKI. However, there has been a long-held belief that PD is unable to achieve adequate clearances to make it comparable with extracorporeal therapies. As a result, there have been concerns that outcomes would be suboptimal in those patients treated with PD. The previous guidelines reviewed this question in-depth and came up with recommendation 1B that acute PD is a suitable modality for treating AKI [18]. After these guidelines, a further single-center randomized controlled trial comparing PD with continuous venovenous hemodiafiltration in critically ill patients was reported and showed a trend towards improved survival in patients treated with PD [8]. A Cochrane review published in 2017 concluded that there is probably little or no difference between PD and extracorporeal therapy for treating AKI with regard to mortality, recovery of kidney function, infectious complications, or correction of acidosis. Fluid removal and weekly delivered Kt/V may be higher with extracorporeal therapy.

Due to the lack of sufficient good-quality clinical data, the choice of dialysis modality should be made according to the patient's clinical symptoms, laboratory examination indexes, and local resources [19].

RECOMMENDATION 2: ACCESS AND FLUID DELIVERY FOR ACUTE PD IN ADULTS

(2.1) Flexible peritoneal catheters should be used where resources and expertise exist **(1B) (optimal).**

(2.2) Rigid catheters and improvised catheters using nasogastric tubes and other cavity drainage catheters may be used in resource-poor environments where they may still be life-saving **(1C) (minimum standard).**

(2.3) We recommend catheters should be tunnelled to reduce peritonitis and peri-catheter leak **(practice point)**.

(2.4) We recommend that the method of catheter implantation should be based on patient factors and locally available skills **(1C).**

Many PD catheters have been developed over the years to address the most common complications associated with PD access namely catheter tip migration, a peritoneal leak, peritonitis, exit-site infection, and catheter entrapment. Despite many innovative designs, no catheter has consistently proven superiority to the double-cuff Tenckhoff catheter. The most appropriate PD catheter is the one that can be positioned deep in the pelvis, can be kept out of reach of the omentum, and can provide an exit site that is easily visible and free of the belt line. Tenckhoff catheters are preferred over rigid catheters as they have a larger diameter lumen and side holes, resulting in better dialysate flow rates and less obstruction, which is imperative in acute PD to achieve adequate clearances. They are also less prone to leakage and have a lower incidence of peritonitis [20, 21]. In addition, the Tenckhoff catheter may provide access to chronic dialysis without additional treatment if kidney function does not improve. All catheters can be inserted under local anesthesia at the bedside or in a surgical theatre. The bedside insertion utilizes a modified Seldinger approach using a guidewire and a peel-away sheath. This is a blind procedure and, therefore, contraindicated in those who have a midline surgical scar or a history suggesting intra-abdominal adhesions. A study by Shanmugalingam et al. from Australia has challenged this rule demonstrating that the use of ultrasound assessment before insertion using the 'slide test' can identify those with previous abdominal surgery who may be suitable for a blind percutaneous insertion [22]. Where death from kidney failure is imminent and no options for ultrasound or direct visualization exist, and PD is the only option, prior surgery could be considered a relative contraindication.

Rigid catheters are inserted using a sharp removable trochar device. Possible complications with this catheter design include bleeding, bowel or bladder perforation, obstruction due to the small side holes and lumen, and leakage of dialysate [20, 23].

Improvised catheter use has been reported in many centers where rigid or Tenckhoff catheters are unavailable. Reported cases describe nasogastric tubes with side holes cut into the tube before insertion surgically. Other options include intercostal drainage tubes, hemodialysis catheters, and percutaneous cavity drainage catheters. It should be noted that none of these options are recommended as the first line; however, they have been shown to be lifesaving, and so it is suggested that they are used if no other option exists [24, 25].

▶▶PD should be considered a suitable modality for the treatment of AKI in all settings◀◀

▶▶Flexible peritoneal catheters should be used where resources and expertise exist◀◀

Table 1. Advantages and disadvantages of flexible, rigid, and other peritoneal access

	Advantages	Disadvantages
Rigid stylet catheter	Inexpensive Can be performed at bedside Easily removed	Frequent catheter dysfunction Flow-related problems Risk of perforation of blood vessels or internal organs
Flexible catheter	Better flow characteristics Less chance of perforation Less leak Less risk of infection Can be performed at bedside	More expensive Requires more training for insertion Risk of catheter tip migration
Nasogastric tubes, hemodialysis catheters, and other drainage catheters	Inexpensive Readily available	Flow related problems Most need surgical placement High risk of leaks Difficulty with achieving reliable connections

(2.5) PD catheter implantation by appropriately trained nephrologists in patients without contraindications is safe and functional results equate to those inserted surgically **(1B).**

(2.6) Nephrologists should receive training and be permitted to insert PD catheters to ensure timely dialysis in the emergency setting **(practice point).**

(2.7) We recommend, when available, percutaneous catheter insertion by a nephrologist should include assessment with ultrasonography **(2C).**

(2.8) Insertion of PD catheter should take place under complete aseptic conditions using sterile technique **(practice point).**

An in-depth review of catheter implantation principles is available in the International Society for Peritoneal Dialysis (ISPD) guidelines on optimal peritoneal access 2019 [26]. The guidelines recommend that one should use a technique that one is most familiar with. A properly implanted catheter ensuring the efficient flow of the dialysate is the prerequisite of adequate dialysis. This depends on the type of catheter used and its location within the pelvis minor, with appropriate preparation of the patient by bowel and bladder voiding being crucial in this regard.

Blind insertion with a Seldinger technique is generally contraindicated in those patients in whom intra-abdominal adhesions might be expected because of the increased risk of bowel perforation. This would include those with a midline laparotomy scar or previous significant peritonitis. Patients with obesity may present technical difficulty and possible infectious complications and, therefore, should be considered for surgical insertion if readily available. Ultrasound evaluation can help in identifying patients in whom the placement of the catheter using the Seldinger method can be safely performed [22]. The procedure should be preferably performed by an experienced clinician in a room specially designed for catheter placement or a sterile, calm environment. Under these conditions, the reported complication rate is low [27–29]. Henderson et al. compared 283 percutaneous with 104 surgically inserted catheters. The incidence of mechanical complications (a leak and poor drainage) was similar between both methods. However, peritonitis within the first month was significantly higher in the surgical group (4% vs. 13%, $p = 0.009$). Perakis et al. reported a higher incidence of a leak occurring in the percutaneous group (10% vs. 2%), but infectious complications were again higher in the surgical group [31]. Al-Hwiesh et al. reported the outcomes of percutaneous catheter insertion without a peel-away sheath with a success rate of above 97.5% [8, 32].

The possibility of PD catheters being inserted percutaneously by appropriately trained nephrologists has a significant practical benefit – it limits the time required from the diagnosis of dialysis requiring AKI to the initiation of treatment, especially if the catheter can be inserted in the emergency room or procedure room instead of waiting for the operating theatre.

The laparoscopic technique allows direct visualization of the peritoneal cavity and placement of the tip of the PD catheter. There is no significant difference in outcomes of laparoscopic versus open surgical placement unless one uses advanced laparoscopic techniques including musculofascial tunneling, omentopexy, and tip suturing [26, 33]. The advantage of laparoscopic insertion over open laparotomy is the relatively small incisions required and the

Table 2. Advantages and disadvantages of different catheter implantation techniques

	Advantages	Disadvantages
Percutaneous method	Can be performed at bedside allowing rapid initiation of dialysis Minimally invasive procedure Physicians or nurses can be trained to perform the procedure Use of ultrasound and fluoroscopy improves implantation outcomes	Risk of bowel or bladder injury (low risk) Not suitable for patients with previous midline surgery or risk of adhesions
Open surgical	Available in most centers Direct visualization of the peritoneum especially important in those with previous midline laparotomy and obese patients Cost of consumables less than laparoscopy	Requires theatre time and anesthetic in most cases Higher incidence of leaks Usually, a catheter is placed blindly in the abdomen, which may result in the catheter not reaching the pelvis
Laparoscopic	Lower incidence of a leak than open surgical Ability to perform an adjunctive procedure such as rectus sheath tunneling and omentopexy A catheter placed in the pelvis under vision	Skilled personnel necessary High costs

ability to suture the port sites thus reducing the risk of a leak in the acute PD patient.

In conclusion, the method of flexible catheter placement should suit the unit, the team's skill set, resources, and cost-effectiveness needs. Table 2 summarizes the advantages and disadvantages of different catheter implantation techniques.

(2.9) We recommend the use of prophylactic antibiotics before PD catheter implantation **(1B)**

The colonization of the Tenckhoff catheter and/or contamination at the time of insertion increases the risk of subsequent peritonitis and needs to be avoided through strict sterile techniques. The most appropriate place for insertion of the catheter will depend on the clinical setting of the patient. For example, in a patient with multi-organ failure and shock, the most appropriate place may be at the bedside in the ICU, whereas a stable patient should be transferred to a surgical theatre, a radiology suite, or a dedicated procedure room. Regardless of the setting, a sterile technique in conjunction with prophylactic antibiotics was shown to reduce the incidence of peritonitis [34–37].

The decision on which antibiotic to use is dependent on local bacterial sensitivities, the ability to achieve sufficient tissue levels (particularly in emergency procedures), and availability. It is generally accepted that the most important organisms to guard against are gram-positive organisms. However, given the small risk of bowel injury, some clinicians use an agent which would also cover gram-negative bacteria.

(2.10) A closed delivery system with a Y connection should be used **(1A) (optimal)**

In resource poor areas, spiking of bags and makeshift connections may be necessary and can be considered **(minimum standard)**

The introduction of Y-sets using a double bag and the disconnect system was one of the most important breakthroughs to reduce the peritonitis incidence rates in chronic patients [38]. Although not formally evaluated, this also applies to PD in AKI patients. To use the disconnect systems, there needs to be an adequate supply of closure devices to ensure that the proximal end of the catheter does not become contaminated between exchanges. If these are not available, it may be safer to leave the 'bag' connected to the patient and perform a 'reverse' exchange (i.e. fill the peritoneum and leave the patient connected for the dwell, then drain and disconnect, attaching the new bag before the next fill).

When commercially produced solutions are not available, then it may be necessary to improvise the system. Some proprietary devices that have a spike system to attach intravenous (IV) fluid containers are available, and this they? can be attached to a three-way tap on the PD catheter with a drainage tube on the other port. If three-way taps are not available, then the fluid can be attached to a standard IV fluid administration set and then used to drain back the fluid. This will only be an option with

flexible plastic bags as they can expand and absorb the excess ultrafiltrate.

(2.11) The use of automated or manual PD exchanges are acceptable and this will be dependent on local availability and practices **(practice point).**

Automated cycler PD is the term used to refer to all forms of PD that employ a mechanized device to assist in the delivery and drainage of dialysate. A volume of dialysate is prescribed as well as the therapy time and fill volume. The advantage of this system is that it can be set up by a trained staff member once per day to reduce the nursing time and probably also the risk of complications. There are conflicting reports of whether there is a reduction in peritonitis with cyclers, but on balance, there appears to be no difference compared to the manual system in chronic PD. This may be different in acute PD where the number of exchanges is increased, hence there is an increase in potential contamination episodes.

In patients who are critically ill, especially those with significant liver dysfunction and marked elevation of lactate levels, bicarbonate containing solutions should be used

Cyclers can be programmed to perform tidal automated PD where a small volume of fluid is left in the abdomen at all times. This may reduce mechanical complications and pain associated with complete fluid drainage. It may have a benefit in critically ill patients because there is always some fluid in contact with the peritoneum, and therefore large molecular weight toxins formed as part of the inflammatory process may be cleared better [40]. This mode has been extensively used for PD in AKI; however, in a resource-poor setting, cyclers may prove too expensive. Good catheter function is also important for the smooth progress of the automatic dialysis, and the previously restricted dialysate flow can be particularly increased upon drainage. Manual exchanges may provide at least a temporary solution to this problem.

Acute PD in patients with acute respiratory distress syndrome or COVID-19 has prompted the question of the **suitability of ….?** in patients in the prone position. There are two aspects to consider. First is the impact of raised intra-abdominal pressure on lung mechanics and organ perfusion. Second is the effect of the prone position on flow characteristics. There are no studies that address this; however, prone positioning increases the intra-abdominal pressure by approximately 1–3 mmHg. Acute PD increases the intra-abdominal pressure approximately by a further 2 mmHg. Intra-abdominal pressures above 18 mmHg should be avoided due to reduced organ perfusion and diaphragmatic splinting; this is unlikely to occur in the absence of other causes of intra-abdominal hypertension (IAH). If IAH is suspected, then the abdominal pressure can be measured. This is most easily performed using a bladder manometer; however, if this is not available, a three-way connector placed between the PD catheter and the PD solution can be connected to a standard vascular pressure transducer. Abdominal pressure in the prone position can be reduced by placing a pillow under the hips and chest, thus allowing the abdomen to be suspended.

As PD catheters in these patients are placed and used acutely, attention to immobilization of the catheter to prevent inadvertent removal is essential.

RECOMMENDATION 3. PERITONEAL DIALYSIS SOLUTIONS FOR ACUTE PD

(3.1) In patients who are critically ill, especially those with significant liver dysfunction and marked elevation of lactate levels, bicarbonate containing solutions should be used **(1B) (optimal).**

Where these solutions are not available, the use of lactate containing solutions is an alternative **(practice point) (minimum standard).**

The high mortality rate among critically ill patients with AKI remains an unresolved problem despite the use of all modes of RRT.

Increasing evidence from clinical studies in adults and children suggests that the new less bio-incompatible solutions may allow for better long-term preservation of peritoneal morphology and function. The formation of glucose degradation products (GDPs) can be reduced and even avoided with double compartment bags allowing separate glucose heat sterilization in an acid environment. Due to the separation of components such as calcium, it is also possible to create solutions whose buffer is bicarbonate and not lactate. Lactate is normally converted to bicarbonate in the liver; however, in critically ill patients and those with liver dysfunction, there is an accumulation of the lactate and the inability to buffer appropriately. A randomized controlled trial including 20 AKI patients compared the effectiveness of bicarbonate versus lactate-buffered PD solutions with a dwell time of 30 min [40]. In shocked patients treated with bicarbonate-buffered solution, there was a more rapid increase in serum bicarbonate (21.2 ± 1.8 vs. 13.4 ± 1.3 mmol/L) and blood

pH (7.3 ± 0.03 vs. 7.05 ± 0.04, $p < 0.05$). These improvements remained statistically significant between the two groups through cycle 36. Overall lactate levels were significantly lower in the groups receiving the bicarbonate-buffered solution in both the patients with shock (3.6 ± 0.4 vs. 5.2 ± 1.3 mmol/L) and without shock (2.9 ± 0.2 vs. 3.4 ± 0.2 mmol/L). However, patients without shock had comparable improvements in both blood pH and serum bicarbonate with either solution [41]. Other outcomes such as hemodynamic stability could not be analyzed because of the limited data available. Results of this study suggest that AKI associated with poor perfusion states should be managed with the use of bicarbonate-buffered solutions if available rather than lactate solutions.

(3.2) Commercially prepared solutions should be used **(optimal).**

However, where resources do not permit this, then locally prepared fluids may be lifesaving and with careful observation of sterile preparation procedure, peritonitis rates are not increased **(1C) (minimum standard).**

Commercial solutions are produced to high standards with strict asepsis and careful monitoring for bacterial and endotoxin contamination. Locally prepared solutions carry potential risks of contamination and mixing errors, which may be life-threatening. The use of hospital pharmacy-prepared solutions has previously been reported in children with good peritonitis rates and outcomes [42–46]. A retrospective review of all acute PD patients showed no difference in peritonitis rates between those treated with commercial solutions and those using locally mixed solutions [44].

Commercial solutions often have closed drainage systems to prevent accidental contamination, whereas makeshift connections may be needed for locally prepared solutions.

Cost is often a factor that may limit the utilization of commercially produced solutions in low-resource settings, particularly if patients are paying for their care. The costs include both the cost of purchasing the solutions and the costs of transportation, taxes, and bureaucratic assessments.

The ISPD recommends the following types of fluid in order of preference:

1. Commercially prepared solutions
2. Locally prepared fluid made in an approved and certified aseptic unit/pharmacy. These products would have a limited expiry time as approved by the manufacturing unit.
3. Solutions prepared in a clean environment with a minimum number of punctures and the least number of steps. This fluid should be used immediately.

(3.3) Once potassium levels in the serum fall below 4 mmol/L, potassium should be added to dialysate (using strict sterile technique to prevent infection) or alternatively oral or intravenous potassium should be given to maintain potassium levels at 4 mmol/L or above **(1C).**

(3.4) Potassium levels should be measured daily **(optimal)**

Where these facilities do not exist, we recommend that after 24 h of successful dialysis, one consider adding potassium chloride to achieve a concentration of 4 mmol/L in the dialysate **(minimum standard) (practice point).**

Losses of potassium can be high in acute PD; such removal may cause serious potassium depletion and cardiovascular instability. This might be prevented or corrected by adding potassium chloride to the dialysis solution to create a solution containing 3–4 mmol/L of potassium. Large studies on PD in AKI patients demonstrated that serum potassium control was obtained after a 24hr session of high-volume PD, and when serum potassium was lower than 4 mmol/L, potassium (K) 3.5–5 mmol/L was added to dialysis solutions to avoid hypokalemia [7, 47]. It is important that the sterile technique is maintained when potassium is added and that nurses are carefully instructed to make certain the amount added is appropriate.

Measurement of potassium on a daily basis is the safest method of monitoring these patients. If this is not possible, it seems prudent to add potassium to the fluid after 24 h. Adding 4 mmol/L of potassium should be safe, although it may limit clearance of potassium from the serum if it is still elevated.

RECOMMENDATION 4: PRESCRIBING AND ACHIEVING ADEQUATE CLEARANCE IN ACUTE PD

(4.1) Targeting a weekly Kt/V urea of 3.5 provides outcomes comparable to that of daily HD in critically ill patients; targeting higher doses does not improve outcomes **(1B).**

This dose may not be necessary for most patients with AKI and targeting a weekly Kt/V of 2.2 has been shown to be equivalent to higher doses **(1B).**

Tidal automated PD (APD) using 25 L with 70% tidal volume per 24 h shows equiva-

Targeting a weekly Kt/V urea of 3.5 provides outcomes comparable to that of daily HD in critically ill patients; targeting higher doses does not improve outcomes

lent survival to continuous venovenous haemodiafiltration with an effluent dose of 23 mL/kg/h **(1C).**

(4.2) Cycle times should be dictated by the clinical circumstances. Short cycle times (1–2 h) are likely to more rapidly correct uraemia, hyperkalaemia, fluid overload, and/or metabolic acidosis; however, they may be increased to 4–6 hourly once the above are controlled to reduce costs and facilitate clearance of larger sized solutes **(2C).**

The concentration of dextrose should be increased and cycle time reduced to 2 hourly when fluid overload is evident. Once the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance

(4.3) The concentration of dextrose should be increased and cycle time reduced to 2 hourly when fluid overload is evident. Once the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance **(1C)**.

(4.4) Where resources permit, creatinine, urea, potassium, and bicarbonate levels should be measured daily; 24h K t/V urea and creatinine clearance measurement is recommended to assess adequacy when clinically indicated **(practice point).**

(4.5) Interruption of dialysis should be considered once the patient is passing > 1 L of urine/24 h and there is a spontaneous reduction in creatinine **(practice point).**

There remains controversy as to the most appropriate dose of PD that should be prescribed for patients with AKI. The factors influencing this are the relative need for small versus large molecule and fluid clearance, the rate of equilibration of molecules, and the relative contribution of convection versus diffusion. Until now, all outcome studies have measured daily/weekly Kt/V_{urea} to assess adequacy. Urea is a small molecule that equilibrates rapidly and with rapid cycling, it will give the impression of adequate clearance. Larger molecules (phosphate, cytokines, etc.) take longer to equilibrate and, therefore, need longer dwell times to achieve this, and clearance of these may be suboptimal despite what appears to be an appropriate dose when measuring Kt/V_{urea}. Creatinine clearance may improve the estimation of larger molecule clearance; however, it is uncertain whether this will be any more appropriate as a target.

For these reasons, one needs to optimize the dwell times once small solutes such as potassium and bicarbonate levels have improved to non-life-threatening levels and aim for dwell times closer to 4 h.

The most effective dose of PD for patients with AKI remains uncertain, mainly due to a limited number of trials, the existence of methodological flaws in some studies, and the fact that the doses of dialysis used varied widely. We also have little knowledge regarding the inter-individual variability of membrane function in critically ill patients. A very small study in infants showed marked differences in Dialysate/Plasma (D/P) creatinine in patients, determined by the cause of the AKI [48].

A study by Ponce-Gabriel et al. compared high-volume PD (36–44 L per session, 18–22 cycles, 2 L per cycle, dwell time 30–55 min) with daily IHD. Approximately 70% of the patients were mechanically ventilated, with a mean acute physiology and health evaluation (APACHE) II score of 25. The patients were randomized to receive a weekly Kt/V of 4.55 (achieved: 3.5) using a cycler, or daily HD with a prescribed K t/V dose of 1.2 (achieved weekly standardized Kt/V: 4.6). Mortality was not significantly different between the two groups (58% and 53%, respectively, p = 0.48) [7].

Other cohort studies have shown very good outcomes with much lower doses (16–24 L per session, 8–16 cycles, 1–2 L per cycle) [9, 49]

The same Brazilian investigators subsequently published a study randomizing 79 patients with AKI on the ICU into groups with different doses of treatment and compared survival. The achieved weekly K t/V was 4.13 in the intensive group and 3.04 in the less intensive group. Mortality was 55% and 53%, respectively (p = 0.72) [49]. This suggests that maybe the target of 3.5 is too high and one could aim lower [15]. It must be noted that, in these studies, the cycle time was very short, which may have had a negative impact on larger molecule clearances. This was not measured in either of these studies, and there is a need for comparative data in this area [50].

The volume of fluid required to achieve the clearances mentioned above would be prohibitively expensive in many of the countries where PD will be used to treat AKI. As a result, the previous ISPD guidelines also recommended a second dosing target of a weekly Kt/V of 2.1. The authors felt that this was the minimum that would be acceptable based on data extrapolated from extracorporeal studies [17].

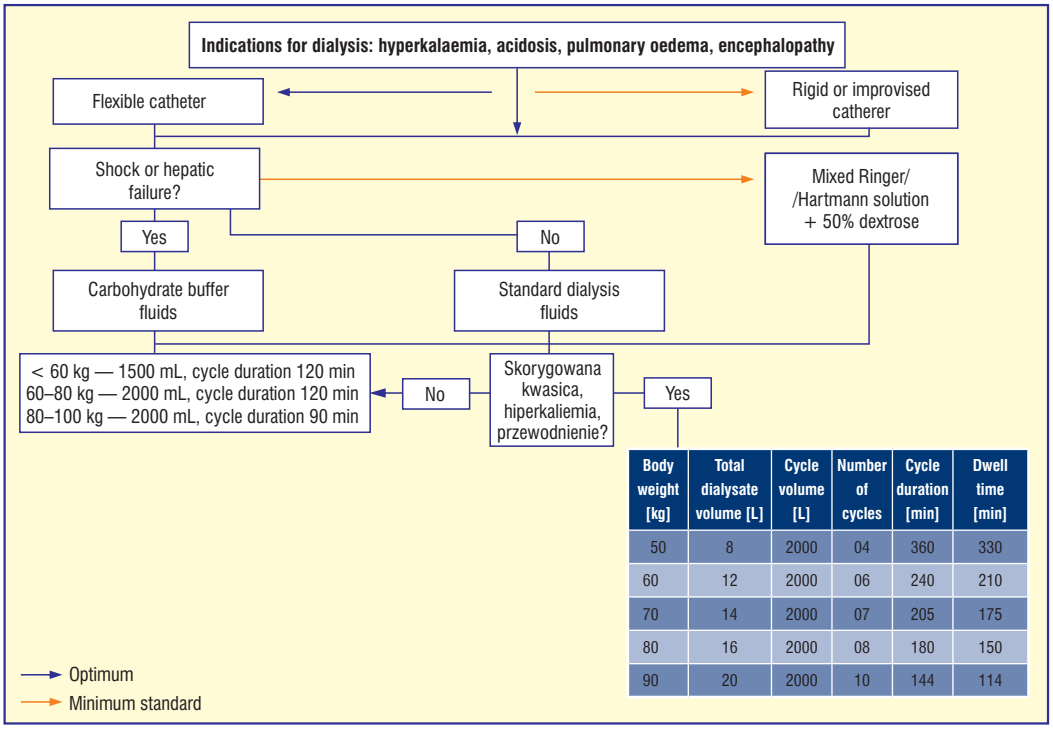
Parapiboon et al. randomized 80 critically ill patients with AKI to 2 regimens recommended in the ISPD guidelines and aimed at achieving target weekly K t/V of 3.5 and 2.1, respectively [52]. Patients were randomized

to receive 1.5 L of PD fluid using manual PD and a single-bag open system delivered either hourly (36 L/24h) or every 2 h (18 L/24h) for the first 48 h. Following this, dwell times were based on metabolic parameters and fluid balance. Catheters were inserted by the nephrologist at the bedside and used immediately. Fluid balance and delivered dose were calculated on a daily basis. Patients were excluded if they had severe hyperkalemia (> 6.5 mmol/L), were hypercatabolic, had chronic kidney disease stage 5, were HIV positive, had recent abdominal surgery, or had a midline scar. The primary endpoint was 30-day mortality, and secondary endpoints were dialysis dependence, metabolic control, peritonitis rate, and length of hospital stay. Baseline characteristics were not significantly different between the two groups. The patients were similar to those in the study by Ponce-Gabriel et al., with 88% on mechanical ventilation, 69% on inotropic support, and a mean APACHE II score of 26. However, the mean body weight was low (Asian population) and blood urea nitrogen (BUN) values were lower than those seen in the Brazilian studies, possibly representing earlier initiation of dialysis. The achieved Kt/V was 2.26 in the low-intensity group and 3.3 in the high-intensity group. There was no significant difference in metabolic control, although ultrafiltration was higher in the high-intensity group. The average glucose concentration in the PD fluid was not reported, making interpretation of the ultrafiltration results difficult. Peritonitis rates were higher in the high-intensity group, albeit non-significant, and despite the use of an open PD system, the overall peritonitis rate was similar to that in the Brazilian study [7, 50]. The mortality was 72% in the high-intensity and 63% in the low-intensity groups ($p = 0.18$), suggesting no advantage to the higher intensity treatment. These results suggest it is unlikely that there is an advantage in achieving a weekly Kt/V > 2.2.

The above studies have used manual or APD with maximum drainage of each dwell. There has been concern raised that the rapid cycling using this method results in significant periods when the peritoneum is not in contact with fluid, thus reducing efficiency. In 2018, Al-Hwiesh et al. published a study randomizing 125 critically ill patients to tidal APD or continuous venovenous hemodiafiltration (CVVHDF). The patients in this study were similar to those mentioned above, with APACHE II scores of 21–22 and > 60% on mechanical ventilation. The volume of fluid used was 25 L/24 h, and it must be mentioned that low GDP, bicarbonate-based solutions were used. Despite the achievement of the target effluent rates of 23 mL/kg/h, serum creatinine levels in the CVVHDF group were lower than expected. The analysis of mortality on the Kaplan-Meier curve showed significantly lower mortality in the tidal APD group (30.2 vs. 53.2%, $p = 0.0028$). This is the first study to demonstrate superior outcomes with PD compared with extracorporeal therapies and needs to be repeated.

Much attention has focused on solute clearances, but there is increasing evidence that fluid overload is also harmful and should be avoided or corrected. In principle, a regular assessment of volume status and the prescription of ultrafiltration and fluid balance targets are necessary for all patients receiving RRT, including PD (53). Relatively large amounts of fluid can be removed by PD, that is, up to 1 L in 2–4 h when using a 4.25% dextrose PD solution. Although this may cause hyperglycemia, the risks of hypertonic solutions are negligible in the short term. The convective clearances associated with this increased ultrafiltration may offer improved middle molecule clearance, and again further research is necessary in this area. Additional attention needs to be paid to the dosing of various medications (such as antibiotics) depending on the peritoneal clearances achieved with acute PD, particularly with high-volume therapy; unfortunately, there is very little in the literature to guide this, but it can be assumed that one would achieve clearances in the order of those seen with daily hemodialysis [54].

RECOMMENDATIONS FOR CLINICAL PRACTICE
1. During the initial 24–48 h of acute PD, the duration of cycle time needs to be determined based on the clinical circumstances (see Fig. 1). Short cycle times (every 1–2 h) may be necessary in the first 24–48 h to correct uremia, hyperkalemia, fluid overload, and/or metabolic acidosis, mainly in critically ill patients and when PD starts late. Thereafter, the cycle time may be increased to 4–6 h depending on the clinical circumstances.
2. To treat or avoid fluid overload, ultrafiltration can be increased by raising the concentration of dextrose and/or shortening the cycle duration. When the patient is euvolemic, the dextrose concentration and cycle time should be adjusted to ensure a neutral fluid balance.



Body weight [kg]	Total dialysate volume [L]	Cycle volume [L]	Number of cycles	Cycle duration [min]	Dwell time [min]
50	8	2000	04	360	330
60	12	2000	06	240	210
70	14	2000	07	205	175
80	16	2000	08	180	150
90	20	2000	10	144	114

Figure 1. The algorithm for suggested management of patients requiring peritoneal dialysis to treat AKI

MANAGING COMPLICATIONS IN PD FOR AKI

There are several potential complications associated with the use of acute PD. Although an in-depth discussion on these is beyond the scope of these guidelines, the following will be discussed briefly: peritonitis, mechanical complications, protein loss, and hyperglycemia.

PERITONITIS

The diagnosis and management of peritonitis in AKI may be challenging but should be based on the recommendations from the ISPD guidelines for infectious complications [55]. The diagnosis is made based on the presence of abdominal pain, cloudy dialysate, and a leukocyte count of > 100 cells μL (or polymorphonuclear cells > 50%) after a 2h dwell. These signs may be masked by the overall illness, and it is, therefore, reasonable to perform a leukocyte count daily for peritonitis surveillance in patients on acute PD. An alternative method is to perform a daily urine leukocyte esterase dipstick test; depending on the outcome, treatment should be initiated while waiting for a confirmatory leukocyte count and cultures. This method has shown good sensitivity and specificity in small studies, but other features such as abdominal pain and fever should also prompt further investigation [56, 57]. Treatment of peritonitis should follow the current ISPD guidelines [55].

MECHANICAL COMPLICATIONS

Mechanical or catheter-related problems are one of the most common problems associated with emergency PD procedures. In one study, this resulted in discontinuation of PD in over 10% of the patients randomized to the PD arm. Ponce et al. studied 204 patients on acute PD and found a mechanical complication rate of 7.3% with interruption of treatment in 2.6% (7).

Catheter flow dysfunction is usually manifested as outflow failure, with constipation being the most common cause (58). This may be manifested as either migration of the catheter out of the pelvis or mechanical obstruction of fluid return to the pelvis. Extrinsic bladder compression on the catheter due to urinary retention occurs less frequently (59). Mechanical kinking of the catheter tubing or an intraluminal fibrin clot is usually accompanied by two-way obstruction.

Primary diagnostic examinations include plain abdominal C-ray which can be used to visualize catheter kinking or displacement, or colon overflow. Treatment of mechanical failure due to constipation involves aggressive attempts to clear the bowel and is usually only achieved with the use of agents reserved

for bowel preparation for colonoscopy. If the abdominal X-ray excludes tubing kinks or displacement, bladder distention is excluded, and flow function is not restored with correction of constipation, then an attempt should be made to repeatedly flush the catheter with 20–50 mL of 0.9% saline. If flushing is unsuccessful, fibrinolytic therapy with tissue plasminogen activator (tPA) may be attempted to clear presumed intraluminal fibrin or blood clots; 8 mL of tPA (1 mg/mL) is slowly injected into the catheter. This can be repeated if there is partial resolution. If catheter obstruction is due to a fibrin or blood clot, the rate of the recovery of flow function with tPA should be nearly 100% [60, 61]. Once the catheter is cleared, then 500 units of heparin should be added to each liter of PD solution. If the catheter has migrated out of the pelvis and there has been no improvement with treating constipation, then the catheter may have been entrapped in the omentum or loops of the bowel. The least invasive method of correction via catheter repositioning is with the use of fluoroscopy and a flexible guidewire to manipulate the catheter into the correct position [62–64]. If fluoroscopy is unavailable or unsuccessful, then surgical options need to be entertained. The least invasive option is to open the midline incision and slowly withdraw the catheter, clean the fibrin out if present, and reintroduce the catheter to the peritoneum using a standard implantation kit. Laparoscopy or minilaparotomy are possible alternatives; these, however, may increase the risk of leakage.

Leakage of peritoneal fluid occurs occasionally. It does not appear to be related to fluid volumes or pressures and may be determined by insertion technique and patient factors. It is recommended that in the first week if a patient is mobilized, they should have a dry or minimally filled abdomen; however, in many cases, these patients are bedridden, and therefore this may not be a common problem. If leakage occurs once the patient is more stable, then it may be possible to rest the abdomen for 24 h and restart PD with smaller volumes. If discontinuation is impossible, then reducing fill volumes may help. Fibrin glue and tissue adhesive have been used in several early leakage cases with some success [65].

METABOLIC COMPLICATIONS

Loss of protein from the peritoneum in patients on chronic PD varies in different studies from 6.2 g to 12.8 g per 24 h. However, this has been known to increase to as high as 48 g during episodes of peritonitis [66, 67]. A study from Brazil measured protein loss in 31 patients on high-volume acute PD over 208 sessions. They showed that protein loss was 4.2 (± 6.1) g/24 h, and there was no correlation with albumin levels. Peritonitis did, however, increase protein loss [68]. Due to the negative impact of negative protein balance on the survival of AKI patients, care should be taken to ensure adequate protein intake (approx. 1.2 g/kg of protein per 24 h) [69].

Due to the high glucose concentration in PD fluid, there is a tendency towards hyperglycemia in acute PD. This decreases the osmotic gradient between PD fluid and serum and should be treated to enable optimal ultrafiltration. Maintenance of normoglycemia has also been shown to significantly improve survival in critically ill patients [70].

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