

In this edition's Editor's Pick, Ponce et al. tackle the various complexities of urgent-start peritoneal dialysis in both acute and chronic kidney failure in light of the current use of haemodialysis, extending their study beyond the controversies and limitations of its use. This in-depth review focusses on the available evidence and guidelines for unplanned chronic dialysis in acute kidney injury, and combines the available evidence to provide a suitable guide to safely prescribing, delivering, and monitoring high volume peritoneal dialysis in patients.

## URGENT START PERITONEAL DIALYSIS: A VIABLE OPTION FOR ACUTE AND CHRONIC KIDNEY FAILURE

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### ABSTRACT

Peritoneal dialysis (PD) may be a feasible, safe, and complementary alternative to haemodialysis, not only in the chronic setting, but also in the acute. Recently, interest in using PD to manage acute kidney injury (AKI) patients has been increasing. Some Brazilian studies have shown that, with careful thought and planning, critically ill patients can be successfully treated with PD. To overcome some of the classic limitations of PD use in AKI, such as a high chance of infectious and mechanical complications, and no control of urea, potassium, and bicarbonate levels, the use of cycles, flexible catheters, and a high volume of dialysis fluid has been proposed. This knowledge can be used in the case of an unplanned start on chronic PD and may be a tool to increase the PD penetration rate among incident patients starting chronic dialysis therapy. PD should be offered in an unbiased way to all patients starting unplanned dialysis, and without contraindications to PD. In the following manuscript, advances in technical aspects and the advantages and limitations of PD will be discussed, and recent literature on clinical experience with PD use in the acute and unplanned setting will be reviewed.

**Keywords:** Peritoneal dialysis (PD), acute kidney injury (AKI), unplanned start.

### THE ROLE OF PERITONEAL DIALYSIS FOR ACUTE KIDNEY INJURY PATIENTS

In the 1970s, acute peritoneal dialysis (PD) was widely accepted for the treatment of acute kidney injury (AKI), but this practice has declined in favour of haemodialysis (HD).<sup>1-4</sup> PD is frequently used in developing countries because of its lower cost and minimal infrastructural requirements.<sup>4-7</sup> However, in developing countries, the infrastructure for quality

research is often lacking, meaning that there has been limited evidence on standardised treatment regimens such as indications, dosing and technical failure, and mortality.

#### Technical Aspects and Controversies

Use of PD in AKI is enhanced by placement of a Tenckhoff catheter by a nephrologist, which can be safely accomplished at the bedside.<sup>8</sup> PD offers several advantages over HD, such as technical

simplicity and a lower risk of bleeding. The gradual and continuous nature of PD ensures that disequilibrium syndrome is prevented and that cardiovascular stress is minimal, which reduces the risk of renal ischaemia and fluid-electrolyte imbalance.<sup>1-8</sup>

Besides the classical indications (volume overload, electrolyte disorders, uraemic symptoms, or acid-base disturbances), PD can also be used to maintain volemic control in patients with congestive heart failure (functional Class IV), and control hyper and hypothermia.<sup>6-10</sup> In the setting of natural disasters, when several victims will develop AKI and damage to infrastructure makes access to power, clean water, and facilities for water treatment unavailable, PD is an important and life-saving renal replacement therapy (RRT) modality.<sup>8-12</sup>

It is also true that PD is not the most efficient therapy: clearance per exchange can decrease if a shorter dwell time is applied, a lower efficiency can be observed in large-sized and severely hypercatabolic patients, fluid removal can be unpredictable, there is a risk of infection, and there are possible issues with mechanical ventilation.<sup>5-15</sup> PD is relatively contraindicated in patients with recent abdominal surgery, abdominal hernia, adynamic ileum, intra-abdominal adhesions, peritoneal fibrosis, or peritonitis. **Table 1** shows the advantages and disadvantages of PD.

Since volume and solute removal is slow and unpredictable, PD is not as efficient as extracorporeal blood purification techniques for the treatment of emergencies such as acute pulmonary oedema or life-threatening hyperkalaemia.<sup>11-17</sup> Another possible limitation of PD in AKI is that associated protein losses may aggravate malnutrition. Protein losses as high as 48 g/day have been reported, but some reports document maintenance of serum albumin levels.<sup>18-21</sup> Protein supplementation, either enteral or parenteral (1.5 g/kg/day) is recommended for AKI patients on PD.<sup>22</sup>

The high glucose concentrations in peritoneal dialysate may cause hyperglycaemia, even in non-diabetic patients. This is easily correctable through intravenous or intraperitoneal administration of insulin.<sup>21</sup> Peritonitis occurring in patients with AKI using PD as a modality of RRT can lead to very poor outcomes, and older studies report a frequency as high as 40%.<sup>2,3,6</sup> With better catheter implantation techniques and automated methods,

the incidence of peritonitis has been reduced and the risk of infection in PD is similar to other forms of extracorporeal blood purification for AKI.<sup>2,3</sup>

Previous studies have reported that PD can increase intra-abdominal pressure (IAP), which leads to impaired diaphragm mobilisation, and decreased pulmonary compliance and ventilation, which may cause or worsen respiratory failure.<sup>22,23</sup> However, PD is seldom the cause of ventilation impairment in patients without pulmonary disease.<sup>24</sup> Results from our group suggest increases in the pulmonary compliance without changes in IAP in AKI patients treated with PD.<sup>25</sup>

## Evidences and Guidelines

Recently, interest in using PD to manage patients with AKI has been increasing. The first question that must be asked is whether PD can provide adequate clearance in the treatment of AKI patients. Our study group, from the Botucatu School of Medicine, Brazil, demonstrated that, with careful thought and planning, critically ill AKI patients can be successfully treated with PD.<sup>2,11,26,27</sup> To overcome some of the classic limitations of PD use in AKI (such as a low rate of ultrafiltration [UF], high chance of infectious and mechanical complications, and no metabolic control) we proposed the use of cyclers, flexible catheters, continuous therapy (24 hours), and high volumes (HV) of dialysis fluid.

We assessed the efficacy of HVPD in a prospective study of 30 consecutive AKI patients.<sup>11</sup> PD was performed using a Tenckhoff catheter, 2 L exchanges, and 35-50 minute dwell times. The prescribed Kt/V value was 0.65 per session, the duration of each session was 24 hours, and a total dialysate volume of 36-44 L/day was used. HVPD was effective in the correction of blood urea nitrogen (BUN), creatinine, bicarbonate, and fluid overload. Weekly Kt/V was 3.8±0.6 and the mortality was 57%. Five years later, we performed another prospective study on 204 AKI patients treated with HVPD (prescribed Kt/V=0.60/session).<sup>27</sup> Sepsis was the main cause of AKI (54.7%) followed by heart failure (24.7%). BUN and creatinine levels stabilised after four sessions to approximately 50 mg/dL and 4 mg/dL, respectively. Weekly-delivered Kt/V was 3.5±0.68 and the mortality rate was 57.3%. Older age and sepsis were identified as risk factors for death. Persistence of urine output, increases of 1 g/day in nitrogen balance (NB), and achieving 500 mL/day

in UF after three sessions were identified as favourable prognostic factors. We concluded that HVPD is effective in selected patients. However, if after three sessions, UF is low or NB is negative, substitution or addition of HD should be considered. There were mechanical complications in 7.3% of AKI patients treated with HVPD and 12% of patients had infectious complications (peritonitis). Change of the dialysis method occurred in 13.3% of patients because of refractory peritonitis or mechanical complications (leakage or UF failure).

Dialysis dose adequacy in AKI is a controversial subject and there are very limited data on the effect of PD dose on AKI. Solute clearance in PD is limited by dialysate flow, membrane permeability, and surface area in contact with dialysate. Exchanges of 2 L lasting approximately 1 hour can achieve a saturation of the spent dialysate in the range of 50%. This means that, over 24 hours, a daily Kt/V of 0.5 can be achieved in a patient with a body weight between 60–65 kg.<sup>2,9-11</sup>

We performed a trial of 61 septic AKI patients randomised to receive higher (n=31) or lower (n=30) intensity PD therapy (prescribed Kt/V of 0.8/session versus 0.5/session). The two groups had similar mortality after 30 days (55% versus 53%, p=0.83). We concluded that increasing the intensity of continuous HVPD therapy does not reduce mortality and does not improve control of urea, potassium, and bicarbonate levels.<sup>28</sup>

According to the International Society for Peritoneal Dialysis (ISPD) guidelines: PD for AKI recommendations, where resources permit, targeting a weekly Kt/V urea of 3.5 provides

outcomes comparable to that of daily HD; targeting higher doses does not improve outcomes. This dose may not be necessary for many AKI patients and targeting a weekly Kt/V of 2.1 may be acceptable.<sup>29</sup>

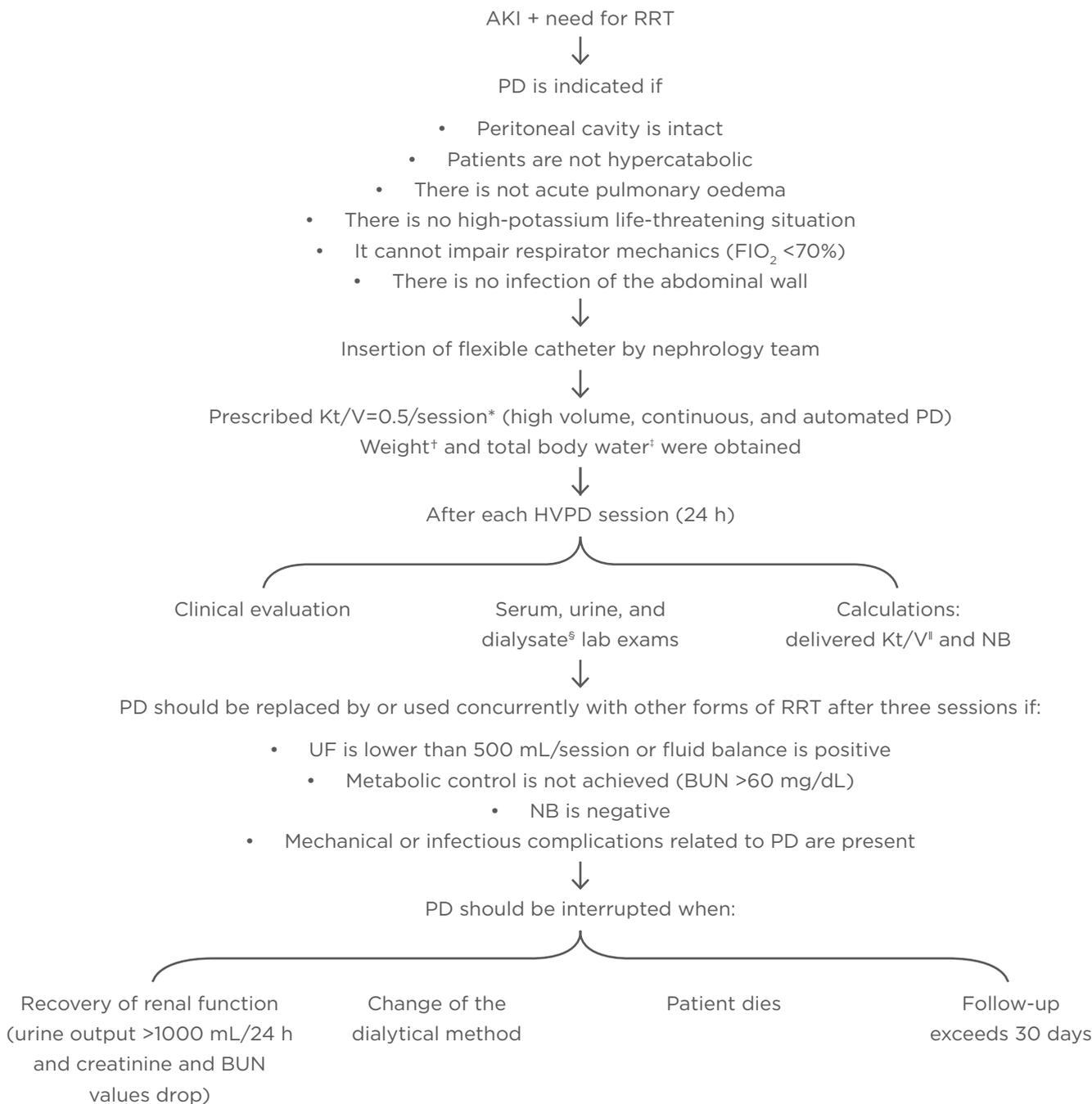
The second question to consider is whether PD is comparable to other dialysis methods in AKI patients. The answer to that question is neither simple nor currently complete. The various modalities present advantages and disadvantages under specific circumstances and these therapies should therefore be considered more as a continuum than as a series of modalities to be compared.<sup>30,31</sup> Few studies have compared PD with other dialysis methods in AKI patients, and reports conflict with regard to efficacy and cost. Phu et al.<sup>16</sup> compared intermittent PD with continuous RRT, and demonstrated a worse outcome in patients treated with PD. Such reports should not be underestimated, although specific factors (such as the use of rigid catheters, manual exchanges, a too-short dwell time [15 minutes], and no dialysis dose quantification)<sup>4,6</sup> might be involved.

A randomised study performed by our group in 120 AKI patients compared HVPD versus daily intermittent HD.<sup>26</sup> Baseline characteristics were similar in both groups, which included older patients (mean age >60 years), patients with a high APACHE II score, and patients using vasoactive drugs (>60%). Both RRT modalities achieved metabolic and acid-base control. Mortality did not differ significantly between the two groups (58% versus 53%). Renal recovery was similar for both modalities, but HVPD was associated with a significantly shorter time to recovery (7.2±2.6 versus 10.6±4.7 days).

**Table 1: Advantages and disadvantages of peritoneal dialysis in acute kidney injury (AKI).**

Advantages	Disadvantages
<ul style="list-style-type: none"> <li>• Technically simple</li> <li>• No need for expensive equipment</li> <li>• Avoids vascular access</li> <li>• Ensures minimal blood loss</li> <li>• Biocompatible</li> <li>• Useful in all types of AKI</li> <li>• Should enhance renal recovery</li> <li>• Provides continuous RRT</li> <li>• Beneficial in select patient populations (children, heart failure, cirrhosis, bleeding diathesis)</li> </ul>	<ul style="list-style-type: none"> <li>• Requires intact peritoneal cavity with adequate membrane function</li> <li>• May not be adequate for severe acute pulmonary oedema or life-threatening hyperkalaemia</li> <li>• Infection (peritonitis) can occur</li> <li>• Ultrafiltration and clearance cannot be exactly predicted</li> <li>• Can cause protein losses</li> <li>• Can cause hyperglycaemia and hypernatraemia</li> <li>• Can impair respiratory mechanics</li> <li>• Lactate buffer</li> </ul>

RRT: renal replacement therapy.



\*Prescribed Kt/V

K = volume of dialysis solution prescribed in 24 hours (mL) × 0.60 (considering the D/P relationship for dwell time between 30 and 60 min); t = 1 (day) and V = patient urea distribution volume (mL).

The number of exchanges was obtained by dividing the K value by 2 L (volume infused in the peritoneal cavity per exchange).

<sup>†</sup>digital scales or two variable formula<sup>42</sup>

<sup>‡</sup>Watson formula<sup>43</sup>

<sup>§</sup>Every day all effluent should be collected to calculate delivered Kt/V and NB. Every 3 days a cell count and cell culture should be performed to diagnose peritonitis.

<sup>¶</sup>Delivered Kt/V

Kt/V = mean dialysate urea nitrogen (mg/dL) / mean serum urea nitrogen pre and post dialysis (mg/dL) × drained 24 h volume (mL) / patient urea distribution volume (mL).

**Figure 1: Flowchart of the practical aspects of prescribing, delivering, and monitoring the HVPD in AKI patients.**

AKI: acute kidney injury; RRT: renal replacement therapy; PD: peritoneal dialysis; HVPD: high volume peritoneal dialysis; NB: nitrogen balance; UF: ultrafiltrate; BUN: blood urea nitrogen.

George et al.<sup>30</sup> performed a randomised study to compare continuous venovenous haemodiafiltration (CVVHDF) and PD in critically ill patients. No difference was observed in correction of metabolic parameters and fluid overload. Urea and creatinine clearances were higher and fluid correction was faster with CVVHDF. The mortality rates in the two study groups were similar. Unfortunately, the procedures were performed at different technological levels to the detriment of PD, in which rigid catheters, locally available PD fluids, and manual exchanges were used.

In another prospective study, we compared the effect of HVPD against prolonged HD (PHD) on AKI patients' outcome.<sup>32</sup> The PHD and HVPD groups were similar in gender, severity, and aetiology of AKI. There was a trend toward statistical difference regarding the presence of sepsis (62.3% in PHD group versus 44.9% in HVPD group,  $p=0.054$ ). Delivered Kt/V and UF were higher in PHD group and there was no difference between the two groups in mortality and recovery of kidney function, or need for chronic dialysis.

A systematic review published by Chion et al.<sup>33</sup> concluded that there is currently no evidence to suggest significant differences in mortality between PD and extracorporeal blood purification in AKI, and that there is a need for high-quality evidence in this important area. Recently, a Brazilian group published the largest cohort study providing patient characteristics, clinical practice, patterns, and their relationship to outcomes in a developing country.<sup>34</sup> Its objective was to describe the main determinants of patient and technique survival, including trends over time of PD treatment in AKI patients.

For comparison purposes, patients were divided into two groups according to the year of treatment: 2004–2008 and 2009–2014. A total of 301 patients were included, though 51 were transferred to HD (16.9%) during the study period. The main cause of technique failure (TF) was mechanical complication (47%) followed by peritonitis (41.2%). There was a change in TF during the study period; patients treated during 2009–2014 had a relative risk (RR) reduction of 0.86 (95% CI, 0.77–0.96) compared with patients treated between 2004 and 2008, and three independent risk factors were identified: period of treatment at 2009 and 2014, sepsis, and age >65 years.

During the study there were 180 deaths (59.8%). Death was the leading cause of dropout (77.9% of all cases), mainly due to sepsis (58.3%), followed by cardiovascular disease (36.1%). The overall patient survival rate was 41% at 30 days and patient survival improved along study periods. Compared with patients treated from 2004–2008, patients treated at 2009–2014 had a RR reduction of 0.87 (95% CI, 0.79–0.98). The independent risk factors for mortality were sepsis, age >70 years, Acute Tubular Necrosis Individual Severity Score (ATN-ISS) >0.65, and positive fluid balance. In conclusion, we observed an improvement in patient survival and TF between the two time periods, even after correction for several confounders and using a competing risk approach. We have prepared a flowchart of the practical aspects of prescribing, delivering, and monitoring the HVPD in AKI patients (Figure 1).

This review clearly shows that PD is a simple, safe, and efficient way to correct metabolic, electrolytic, acid-base, and volume disturbances generated by AKI; it can be used as a RRT modality to treat AKI, either in or out of the intensive care unit setting. We have recently observed an improvement in patient and technique survival over the years even after correction for several confounders.

## THE ROLE OF PERITONEAL DIALYSIS FOR UNPLANNED INITIATION OF CHRONIC DIALYSIS

Although historically PD was widely used in nephrology, for reasons that are unclear it has been underutilised in recent years. Possible reasons for this include the 'perception' that it is inferior to HD, which is associated with greater technology; the infectious, mechanical, and metabolic complications associated with PD; the higher financial reimbursement with HD use; and difficulties with catheter peritoneal insertion.<sup>35,36</sup>

In 2007, there were 368,000 prevalent patients on RRT in the USA, 92.8% of whom were on HD.<sup>37</sup> Data from 2013 has shown that in Brazil, 90.6% of chronic patients underwent HD and only 9.4% were treated by PD.<sup>38</sup> Several studies have compared the differences between the two types of dialysis, PD versus HD, in incident patients on RRT. There is no evidence of the superiority of one method over the other in regard to general mortality within the first 2 years of therapy.<sup>39–44</sup> Some studies have demonstrated better results with PD in young

patient groups with no comorbidities, while other studies have shown lower mortality after 2 years of dialysis in elderly patients with comorbidities treated by HD.<sup>40-42</sup>

Some authors have recently highlighted the impact that the use of vascular access has in the mortality of incident patients in HD.<sup>40,41</sup> These studies found that central venous catheter (CVC) use is associated with reduced survival, especially in the first 90 days of RRT. Furthermore, there is a greater risk of bacteraemia, sepsis, and hospitalisation in patients using CVC when compared with patients using arteriovenous fistulas or PD.<sup>45-47</sup>

In this scenario, PD appears as an option in unplanned initiation of chronic dialysis. Advantages of PD include the lack of CVC use, thereby preserving vascular access and residual renal function, which can reduce the morbidity and mortality of these patients.<sup>35,46,47</sup> Most patients with end-stage chronic kidney disease (CKD) start unplanned RRT.<sup>48-50</sup> Ivarsen et al.<sup>45</sup> retrospectively reviewed the Danish Registration Nephrology from 2008-2011 and found that 50% of incident patients on RRT started the treatment in an unplanned manner. In Brazil, approximately 60% of incident patients on RRT have no definitive access and need to be treated through CVC. In the dialysis unit of the University Hospital of the Botucatu Medical School, the reality is worse than in the rest of the world: more than 90% of the incident patients start unplanned dialysis and 60% of prevalent patients have no functioning vascular access and are treated through CVC.<sup>49,50</sup> Unplanned dialysis may be defined as the start of HD without functioning definitive vascular access, i.e. using CVC, or as the start of PD <7 days after its implantation.<sup>45-50</sup> This situation is common even for patients who have attended a previous follow-up with a nephrologist.

## Evidence

There are few studies that describe the PD method as an immediate treatment option in patients without functioning vascular access and only two small studies that compared unplanned start of HD versus PD.<sup>46-47</sup> These studies showed that there was no significant difference in the mortality rates between the two methods.

Lobbedez et al.<sup>47</sup> followed 60 patients who started unplanned dialysis for a 2-year period. Among the patients who started on PD, only

two had mechanical complications after catheter implantation and showed no significant difference in mechanical or infectious complications when compared with patients who had 'rest time' post catheter insertion. There was no significant difference in patient survival between the two unplanned dialysis methods (78.8% versus 82.9%,  $p=0.26$ ).

Koch et al.<sup>46</sup> evaluated 57 incident patients in unplanned HD and 66 in unplanned PD. HD patients had a higher rate of bacteraemia than PD patients in the first 6 months of dialysis (21.1% versus 3%,  $p<0.01$ ), which was associated with the use of CVC as initial access. However, there was no significant difference in the mortality rates between the two methods.

Danish data support the idea that early unplanned PD is associated with lower risk of infectious complications compared to the incident HD patients using CVC.<sup>48</sup> The authors noted that there was a higher number of cases of catheter-related mechanical complications in patients starting unplanned PD compared with those who had 'rest time' after implantation of the peritoneal catheter, although it did not affect the method or patients' survival.

Since July 2014, we have offered PD as urgent start for chronic patients. We evaluated our first year of experience<sup>51</sup> concerning technique and patient survival on unplanned PD in the first 90 days. In this prospective study we described how acute PD was initiated right after (<48 hours) PD catheter placement using HVPD until metabolic and fluid control were achieved. After hospital discharge, patients were treated by intermittent PD on alternate days at the dialysis unit until family training. Fifty-five patients were included from July 2014 to July 2015. The mean age was  $57.7\pm 19.2$  years, diabetes was the main aetiology of CKD (40.6%), and uraemia was the main dialysis indication (54.3%). Metabolic and fluid controls were achieved after five sessions of HVPD and patients remained in intermittent PD for  $23.2\pm 7.2$  days and received  $11.5\pm 3.1$  intermittent PD sessions. Peritonitis and mechanical complications occurred in 14.2% and 25.7% of patients, respectively, within 90 days. The mortality rate was 20% and technique survival was 85.7% in the first 90 days. The chronic PD programme presented growth of 79%. We concluded that the concept of urgent start on chronic PD may be a feasible, safe, complementary alternative to HD, and a tool to increase the PD

penetration rate among incident patients starting dialysis therapy. Although data on unplanned initiation of PD are scarce, they indicate that mortality is the same or even better than in cases of unplanned initiation of HD, and that the number of infectious complications including bacteraemia appear lessened.<sup>45-47,51</sup> It is clear that PD is a suitable method for unplanned dialysis patients and that acute automated PD may help nephrologists to deal with patients without any permanent vascular access at dialysis initiation.

To conclude, our observations suggest that the PD modality may be a feasible and safe alternative to HD not only in planned, but also in urgent start. Moreover, the concept of unplanned start on chronic PD may be a tool to increase the PD penetration rate among incident patients starting chronic dialysis therapy. Urgent-start PD is an option and should be offered in an unbiased way to all patients without contraindications to PD starting unplanned dialysis.

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