

## Peritoneal dialysis as the first dialysis treatment option initially unplanned

Diálise peritoneal como primeira opção de tratamento dialítico de início não planejado

### Authors

Marcela Lara Mendes <sup>1</sup>

Camila Albuquerque  
Alves <sup>1</sup>

Edwa Maria Bucovic <sup>1</sup>

Dayana Bitencourt Dias <sup>1</sup>

Daniela Ponce <sup>1</sup>

<sup>1</sup> Universidade Estadual Paulista Júlio de Mesquita Filho (UNESP), Faculdade de Medicina, Botucatu - SP, Brazil.

### ABSTRACT

Most patients with stage 5 CKD start RRT of unplanned manner. Unplanned dialysis, also known as urgent start, may be defined as hemodialysis (HD) started without permanent vascular access, i.e., using a central venous catheter (CVC), or as peritoneal dialysis (PD) started within seven days after implantation of the catheter, without family training. Although few studies have evaluated the PD as an immediate treatment option for patients starting urgent RRT, their results suggest that it is a feasible and safe alternative, with infectious complications and survival similar to patients treated with unplanned HD. Given the importance of the social role of urgent start of dialysis and the lack of studies on the subject, this narrative review aims to analyze and synthesize knowledge in published articles, preferably, from last five years in order to unify information and facilitate future studies.

**Keywords:** hemodialysis units, hospital; peritoneal dialysis; renal insufficiency, chronic; renal replacement therapy.

### RESUMO

A maioria dos pacientes com DRC estágio 5 inicia terapia renal substitutiva (TRS) de modo não planejado. A diálise não planejada, também conhecida como de início urgente, pode ser definida como hemodiálise (HD) iniciada sem acesso vascular definitivo (utilizando cateter venoso central) ou como diálise peritoneal (DP) iniciada dentro de 7 dias após o implante do cateter. Embora poucos estudos tenham avaliado DP como opção de tratamento imediato em pacientes que iniciam a TRS de modo urgente, seus resultados sugerem que é alternativa viável e segura, apresentando complicações infecciosas e sobrevida semelhantes às dos pacientes tratados por HD não planejada. Tendo em vista a relevância do papel social do início não planejado da TRS e a escassez de estudos sobre o tema, a presente revisão narrativa propõe analisar e sintetizar conhecimentos fragmentados em artigos publicados, no período de 5 anos com o intuito de unificar informações e facilitar estudos futuros.

**Palavras-chave:** diálise peritoneal; insuficiência renal crônica; terapia de substituição renal; unidades hospitalares de hemodiálise.

### AN OVERVIEW ON CHRONIC KIDNEY DISEASE

Chronic kidney disease (CKD) is a serious global public health issue. The global number of patients treated with dialysis and kidney transplantation is expected to grow substantially.<sup>1,2</sup> According to Lugon *et al.*,<sup>3</sup> the world is facing an epidemics of CKD and the number of patients is growing more significantly in developing nations.

In the United States of America (USA), the number of individuals with CKD is estimated to grow from 470,000 in 2004 to more than 2.2 million in 2030.<sup>4</sup> In Brazil, the annual census published by the Brazilian Society of Nephrology (SBN) revealed that 65,121 patients were on dialysis in 2005,<sup>5</sup> versus 91,314 in 2011 and more than 112,000 in 2014.<sup>5,6</sup> The rate of incident patients on dialysis was 119 per million population (ppm) in 2005, 149 in 2011, 161 in 2013, and 180 in 2015.<sup>5,6</sup>

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### Correspondence to:

Marcela Lara Mendes.  
E-mail: mazinha26@yahoo.com.br

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The dialysis modes available to nephrologists are peritoneal dialysis (PD) and hemodialysis (HD), the latter being the most frequently used method.<sup>7</sup> PD has been broadly used historically, and for unclear reasons it has not been prescribed as often in recent years. Possible explanations include the perception that PD is inferior to HD, since HD is seen as a technologically more developed treatment, fear of infection, metabolic and mechanical complications associated with PD, trouble placing the peritoneal catheter, and the lower reimbursement paid for PD by health maintenance organizations.<sup>7,8</sup>

In 2013, 661,648 individuals were on RRT in the USA, 63.7% on HD and 6.8% on PD.<sup>9</sup> In Brazil, data from 2014 revealed that 91.4% of the individuals with CKD were on HD, while only 8.6% were offered PD.<sup>7</sup>

Several studies have compared the clinical outcomes of patients treated with PD and HD, and to this day no evidence of superiority of one method over the other has been reported in terms of overall mortality within the first two years of therapy.<sup>7,10</sup>

Subgroup analysis has revealed improved outcomes with PD in younger patients without comorbidities, while lower mortality rates have been reported for elderly patients with comorbidities treated for two years with HD.<sup>8,11</sup>

In recent years, some authors have described associations between the type of vascular access and mortality in incident patients on HD.<sup>11,12</sup> These studies reported that the use of a central venous catheter (CVC) is directly linked to decreased survival, particularly within the first 90 days of therapy. Additionally, greater risk of bacteremia, septicemia, and hospitalization has been described for patients using a CVC when compared to individuals equipped with arteriovenous fistulae (AVF), grafts or PD.<sup>7,11,12</sup>

In this setting, PD appears to be an option when a patient has to be urgently started on chronic dialysis. PD offers the benefit of not requiring a CVC, thus preserving the vascular access and residual renal function, while possibly reducing patient morbidity and mortality.<sup>13,14</sup>

#### **PERITONEAL DIALYSIS AS THE METHOD OF CHOICE TO URGENTLY START THERAPY**

Unplanned start dialysis, also known as urgent-start dialysis, may be defined as the initiation of HD without a definitive functioning vascular access - i.e.,

treatment is started with a CVC - or the start of PD within seven days of the implantation of a catheter.<sup>15,16,17</sup>

Iversen *et al.*<sup>15</sup> retrospectively reviewed the Danish Nephrology Registry (2008-2011) and reported that 50% of the incident patients on RRT had unplanned therapy starts. In Brazil, approximately 60% of the incident patients on RRT do not have a definitive access and are treated with a CVC. In the dialysis center of the University Hospital of the Medical School of Botucatu (Hospital Universitário da Faculdade de Medicina de Botucatu), the numbers are even more alarming: more than 90% of the incident patients have unplanned dialysis starts and 50% of the prevalent patients do not have a definitive functioning vascular access and are treated with tunneled CVCs.<sup>16,17</sup>

In a recently published paper, Lok *et al.* reported that about a third of the patients worldwide have unplanned RRT starts, an event that makes the discussions around the development of diagnosis and treatment, including the choice of mode of dialysis and the implantation of a dialysis access, more challenging to the health care team.<sup>18</sup>

PD has been seen as a viable and safe alternative to HD in unplanned dialysis starts in developed and developing nations, nurturing the growth of PD programs.<sup>19,20,21,22,23</sup>

Casaretto *et al.*<sup>24</sup> and Ghaffari *et al.*<sup>25</sup> reported that urgent-start PD programs call for novel infrastructure and specific care processes. The medical team has to be ready and available to implant peritoneal catheters in emergency settings, with the active participation of nephrologists. Changes to the infrastructure of PD units are needed so that dialysis can be offered to patients, while nursing, administrative, and dialysis staff involvement plays a pivotal role in the development of catheter implantation, dialysis prescription, and nurse training protocols.

The participation of nurses in the training of patients and their families is of the utmost importance for the success of PD therapy. However, few nurses have specialized on PD and fewer studies have looked into the impact of proper training on patient and catheter survival.<sup>26,27</sup>

Figueiredo *et al.*<sup>26</sup> published a study whose purpose was to assess the impact of training over rates of peritonitis in a large Brazilian cohort (BRAZPD II) from January of 2008 to January of 2011. Patients given more than 15 hours of training had significantly lower incidence of peritonitis when compared to

individuals trained for fewer than 15 hours (0.26 vs. 0.32 episodes a year,  $p = 0.01$ ). The presence of a caretaker and the number of people trained were not significantly associated with incidence of peritonitis. Training delivered before catheter implantation or ten days after implantation was associated with lower rates of peritonitis when compared to training initiated within the first ten days of catheter implantation (0.28 vs. 0.23 vs. 0.32 episodes a year, respectively;  $p = 0.003$ ). This was the first study to analyze the association between training characteristics and infection outcomes in a large cohort of patients on PD. The authors concluded that training programs lasting fewer than 15 hours, smaller dialysis centers, and start of training program within fewer than 10 days of catheter implantation were associated with increased incidence of peritonitis.

When PD is initiated in an unplanned manner, the time and quality of the training delivered to patients and their caretakers must consider recent evidence.

#### CLINICAL TRIALS ON THE USE OF PD IN UNPLANNED DIALYSIS STARTS

Few studies have looked into PD as an option to urgently start the treatment of patients without a functioning vascular access.<sup>12,16,17</sup> Table 1 summarizes the main characteristics of these trials.

Lobbedez *et al.*<sup>20</sup> followed 60 patients with unplanned dialysis starts for two years, 34 treated with PD and 26 with HD. Only two of the patients treated with PD had mechanical complications related to catheter implantation. No significant differences were found for mechanical complications or infection when they were compared to patients who enjoyed a rest period after catheter implantation, i.e., individuals with planned dialysis starts. The survival of patients with unplanned starts treated with PD and HD was similar (78.8% in the HD group vs. 82.9% in the PD group,  $p = 0.26$ ).

Koch *et al.*<sup>19</sup> studied 57 incident patients with unplanned starts given HD and 66 offered PD. HD patients had more bacteremia than PD patients within the first six months of dialysis (21.1% vs. 3%,  $p < 0.01$ ), a finding associated with the use of CVCs as the mode of initial access. The two groups had similar death rates.

Danish data reinforce the idea that PD in unplanned start dialysis is associated with lower risk of infection when compared to urgent-start HD with a CVC.<sup>15,28</sup> In 2009, Povlsen *et al.*<sup>28</sup> described the initial results of an unplanned starts using PD. The data revealed that unplanned dialysis starts with PD did not result in inferior time free of peritonitis, catheter or patient survival when compared to planned start PD. However, increased risk of mechanical complications and more catheter replacements were observed. The authors concluded that PD is a viable, safe, and efficient option in unplanned therapy starts.

The same authors saw more catheter-related mechanical complications in unplanned PD starts than in individuals given rest periods before peritoneal catheter implantation. However, higher prevalence of mechanical complications was not related to poorer patient or catheter survival.

Alkathoori *et al.*<sup>29</sup> recently described the initial Canadian experience with urgent-start peritoneal dialysis. In a prospective observational study, the authors followed 30 incident patients on PD with unplanned starts and analyzed cases of mechanical complications and infection. Three patients (10%) had pericatheter leaks within the first week of treatment without therapy interruption. Cases of peritonitis or exit-site infection were not observed within the first four weeks of catheter implantation. Six individuals (20%) had mechanical catheter dysfunction (migration), corrected with catheter repositioning; no catheters had to be changed or patients switched to other therapies. The authors concluded that urgent-start PD is an effective and safe alternative for patients without a functioning HD access needing to start dialysis urgently.

In 2014, Liu *et al.*<sup>30</sup> reviewed and compared the cost associated with *urgent-start PD*, urgent-start HD, and the dual approach (urgent-start HD followed by urgent-start DP) throughout the first 90 days of treatment. The estimated cost per patient for the first 90 days of urgent-start PD was USD 16,398, versus USD 19,352 and USD 19,400 for urgent-start HD and the dual approach (urgent start HD+PD), respectively. The authors concluded that PD is more cost effective than HD in unplanned therapy starts.

**TABLE 1** MAIN CHARACTERISTICS OF RECENT STUDIES ON UNPLANNED PD START

Study	Year	Patient group	Planned vs. unplanned therapy	Results	Complications
Lobbedez <i>et al.</i> <sup>20</sup>	2008	34 PD and 26 HD	Unplanned PD vs. unplanned HD	No significant difference between groups in patient survival (78.8% in the HD group vs. 82.9% in the PD group).	Only two cases of mechanical complication after catheter implantation
Koch <i>et al.</i> <sup>19</sup>	2012	57 incident patients on unplanned HD and 66 on unplanned PD	Unplanned HD vs. unplanned PD	No significant difference between groups in death rates (n = 20 PD patients (30.3%) vs. n = 24 HD patients (42.1%) <i>p</i> = 0.19)	HD patients had more bacteremia than PD patients within the first months of dialysis - associated with the use of CVCs as initial access (21.1% vs. 3%, <i>p</i> < 0.01)
Povlsen <sup>26</sup>	2009	20 incident patients on planned PD and 19 on unplanned PD	Planned PD vs. unplanned PD	No significant difference between groups in patient survival or time without infection	Risk of mechanical complications and need to change peritoneal catheter were greater in the unplanned PD group
Alkathheeri <i>et al.</i> <sup>29</sup>	2014	30 incident patients on PD	Urgent-start PD	The authors concluded that urgent-start PD is a safe alternative for patients without a hemodialysis access needing to start dialysis urgently	Three patients (10%) had leaks; six patients (20%) had catheter migration, corrected by repositioning the catheter without the need to replace the catheter or change the mode of therapy.
Liu <i>et al.</i> <sup>30</sup>	2014	Five clinics offering urgent-start HD or DP. 218 patients had unplanned starts - 95 on PD, 97 on HD, and 26 on the dual approach (urgent-start HD+PD)	Urgent-start PD, urgent-start HD, and dual approach (urgent-start HD followed by urgent-start PD)	The authors concluded that urgent-start PD is cost-effective. The estimated cost per patient for the first 90 days of urgent-start PD was USD 16,398 vs. USD 19,352 for urgent-start HD.	None
Dias <i>et al.</i> <sup>23</sup>	2016	35 incident patients on unplanned PD; the first 90 days of therapy	Unplanned PD	Metabolic management as achieved after five high-volume PD sessions; patients remained on IPD for 23.2 ± 7.2 days and had 11.5 ± 3.1 IPD sessions. Death rate was 20%; catheter survival rate was 85.7%. Chronic PD program grew by 41.1%.	Peritonitis and mechanical complications occurred in 14.2% and 25.7% of the cases, respectively.

PD: peritoneal dialysis; HD: hemodialysis.

Dias *et al.*<sup>23</sup> published the early results of a study carried out by our group, including 35 patients seen from July of 2015 to January of 2015. The patients had a mean age of 57.7 ± 19.2 years, diabetes was the main etiology of CKD (40.6%), and uremia was the main reason for the prescription

of dialysis (54.3%). Metabolic management was achieved after five high-volume PD sessions, and the patients remained on intermittent PD for 23.2 ± 7.2 days had 11.5 ± 3.1 sessions of intermittent PD. Peritonitis and mechanical complications occurred in 14.2% and 25.7% of the cases, respectively. The

reported death rate was 20%, and catheter survival rate was 85.7%. The chronic PD program grew by 41.1%. Unplanned chronic PD may be a viable and safe alternative, a complement to hemodialysis, and a tool to popularize PD programs with incident patients started on dialysis.

Although data on unplanned PD starts is still scarce, there is indication that patients with unplanned HD starts have similar death rates and more infection, including bacteremia.<sup>15,17,20</sup>

Clinical trials comparing unplanned HD *vs.* unplanned PD starts will hardly ever be carried out because of their ethical implications. Therefore, observational studies of good quality performed in developed and developing nations must be carried out to further support urgent-start PD.

Studies carried out to date suggest that PD is a viable and safe alternative for patients with unplanned dialysis starts, in addition to being a useful tool to increase the prevalence of patients treated with chronic PD. Therefore, PD is an option that should be impartially offered to patients without treatment contraindications needing to start dialysis urgently.

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