Getting the Right Patient on the Right Renal Replacement Therapy

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Abstract
Adequate selection of the modality of renal replacement therapy (RRT), ideally based on well-planned predialysis care, informed decision by the patient and timely initiation of dialysis, is essential to optimize the outcome of patients with chronic kidney disease. However, there are important practical limitations to the success of this process. A major consequence is the underutilization of home-based dialysis therapies, including peritoneal dialysis (PD). A wide array of medical and social factors have been invoked as contraindications to PD, but well-designed studies have shown that most patients (probably >70%) starting dialysis are suitable for this technique. PD is feasible and may be preferred by a significant proportion of patients in many claimed unfavorable settings. The practicing nephrologist should be able to: disclose which are insurmountable barriers to PD, clarify the significance of relative contraindications in individual cases, and identify favorable and unfavorable settings for home dialysis. These abilities will permit quality education, justified advice, well-targeted informed decision and, predictably, successful selection of the modality of RRT. This article provides some clues to approach these issues in three different settings: planned start of RRT after predialysis care, unplanned start of dialysis and programmed changes of modality during follow-up.

Management of end-stage kidney disease (ESKD) demands systematic approaches to optimize care and limit the economic burden of renal replacement therapies (RRT). An integra- tive view of the different modalities is essential to ensure that patients may benefit from the best possible therapy during their progress. This itinerary must start before the initiation of dialysis. All individuals with advanced chronic kidney disease (CKD) should undergo structured predialysis care, oriented to delay the progression of CKD, prevent its complications and, importantly, permit education on the characteristics of different techniques of RRT, oriented to select the most appropriate and prepare the patient for its initiation. On the other hand, the right to informed decision should not stop with the start of RRT, because changes in the circumstances of the patient can make convenient a mode of RRT different to the initially chosen.

In the present article, we shall give some clues to help patients target their most convenient modality of RRT in three different scenarios.

Targeting RRT in the Patient Receiving Predialysis Care

This favorable setting permits a fruitful cooperation between the patient, his/her relatives and the attending team to select the most convenient modality of RRT. In some cases, usually associated with a short life expectancy or irreversible loss of the quality of life, the choice will be conservative management. A small proportion of individuals will have access to preemptive kidney transplan- tation (KT). Finally, in the majority of cases dialysis will be the only possible path. A proportion of patients in this latter group will still be eligible for KT but, even in these, dialysis will be necessary for variable, often prolonged periods of time.

An important issue at the time of planning modality selection is that information and advice should be objective and, whenever possible, based on scientific evidence, but not necessarily neutral. Of course, the educator has the right to manifest his preferable option, but must present orderly clinical and social arguments to support the recommendation. Unfortunately, and despite the abundance of information oriented to facilitate these decisions, many issues remain controversial, due to a paucity of quality evidence.

Many nephrologists still have a perception that a majority of ESKD patients present clinical or social contraindications to home dialysis, including peritoneal dialysis (PD), and that the latter technique is globally inferior to hemodialysis (HD) [1,2]. However,

well-designed studies have shown that more than 70% of patients starting RRT are suitable for PD, as compared with 95% in the case of HD [3–5]. Moreover, PD and HD appear globally equivalent in terms of patient survival. Remarkably, the last years have contemplated a significant improvement in the results reported for PD, driven by technical advances and the maturity gained during the 1990s. Current registry data suggest that the comparability between PD and HD persists now at least until the fifth year of follow-up [6,7]. Technique survival is still lower in PD although, in this case too, results have improved markedly, and median survival rates of five years or more are now a realistic target. On the other hand, for decades PD has suffered the label of infection-prone technique. The progressive decrease in the incidence of peritoneal infections and the excess use of central venous catheters (CVC) for HD has reversed this situation, and CVC-related bacteremia is currently the main infectious threat to dialysis patients [8]. There is no evidence of a generic superiority of either PD or HD in terms of quality of life [9]. The latter depends more likely on a right modality selection than on the modality itself.

Absolute Contraindications and Indications for PD

There are few unquestionable medical contraindications for PD. These include lack of a suitable peritoneal membrane (extensive surgical resection, peritoneal sclerosis), inability of the abdominal cavity to sustain the mechanics of the process (peritoneal compartmentalization, uncorrectable hernias or pleuroperitoneal leaks) or conditions bringing an unacceptable risk of infection (active inflammatory bowel disease, recurrent diverticulitis). Social contraindications are more frequent in clinical practice. Refusal by the patient to take on self-care is the most common one. This argument is currently challenged in some countries due to financial constraints [10] but, in general, few nephrologists would pressure a patient who overtly rejects self-care dialysis. The combination of an inability for self-care and lack of support by either relatives or the health care system is another insuperable barrier to home dialysis selection. On the other hand, aside from the unusual case of an impossibility to sustain any type of vascular access, there are few unequivocal medical or social indications for PD.

Controversial Contraindications and Indications for PD

Some patients suffer medical conditions which may interfere with the success of PD, but should not be considered generic contraindications to this technique. Adult polycystic kidney disease may compromise PD through complicated catheter insertion, increased prevalence of hernias and diverticulosis or inability to meet adequacy targets, due to the conflict of space created by the enlarged kidneys. However, PD has been used extensively in this condition [11], and should probably be discouraged only in patients who associate giant kidneys with other risk factors for inadequacy (e.g. large patients with absent residual renal function RRF) or mechanical complications (e.g. recurrent hernias).

Morbid obesity is often quoted as a contraindication to PD, due to complicated catheter insertion, increased risks of hernias and infections, and worsening metabolic derangements. Despite these drawbacks, there is no consistent evidence that PD is inferior to HD in these patients [12].

Former claims about the inconvenience of PD to treat ESKD individuals with advanced cirrhosis and ascites were based on the potential risks of peritoneal infection and worsening malnutrition (protein leak). However, this technique also permits a gentle control of volemia and alleviates tense ascites in these patients. Clinical experience supports the use of PD in this setting [13].

Diverticulosis has been claimed to confer an increased risk of enteric peritonitis, but this fear has not been clearly substantiated by clinical experience. Chronic obstructive pulmonary disease, lumbar spine disorders or malnutrition may deserve specific prescription strategies, but do not represent contraindications to PD. Other less-frequent medical conditions which may hamper the use of PD include ostomies, recurrent correctable hernias or dormant inflamma- tory bowel disease.

There are some relative social contraindications to PD. Patients with a background of noncompliance, limited ability for self-care and poor family support, or unstable home conditions should be carefully evaluated with the help of social workers and psychologists before home dialysis is considered.

Some medical reasons to recommend PD over HD in the predialysis stage include recurrent thrombosis of planned vascular accesses, hypercoagulability syndromes, antecedents of cholesterol embolism or bleeding diatheses. Long distance to the nearest

HD center, poor mobility or convenience of a stable home environment (e.g. children) are frequently quoted, relative social indications for PD.

Favorable and Unfavorable Settings for PD

Well-planned predialysis care followed by informed decision is, undoubtedly, the most important factor for selection of PD by patients incident on RRT, as shown by different registry [3,14–16] and cohort studies [5,17], and even randomized trials [18]. In general, attempts to predict from demographic data which patients will be inclined to home dialysis have found a limited success. Male sex, pediatric age, low comorbidity, motivated individuals with an interest in an independent lifestyle, active workers, persons with a high educational level, and availability of family support have all been quoted as conditions favoring home PD, while older age, comorbidity and lack of family support are common arguments to prefer in-center HD [3,5,14,19,20]. PD and home HD patients also present differentiated patterns [20]. Overall, the predictive capacity of these profiles is poor and they cannot substitute individual informed decision.

In patients with ESKD and no apparent con- traindication for any modality of RRT, predialysis education should include the proposal of an orderly planned RRT. This integrative approach to RRT [21] has a natural extension in the 'PD-first' strategy [22]. The seminal argument is the time-dependent risk relationship between PD and HD, the former yielding better results dur- ing the first years of RRT. In addition, PD is particularly fit for initiation with low-dose schedules (incremental prescription), which optimize qual- ity of life and decrease the economic cost of therapy. Later on, many patients will still do well on PD while, for those announcing complications such as inadequacy or membrane dysfunction, a timely change to HD will permit continuation of quality RRT. There is some evidence that this strategy provides better outcomes than HD-only approaches [21]. On the contrary, late transfer to PD of patients previously treated with HD is feasible, but yields poorer results. The reasons are not totally clear, but better preservation of RRF and greater dependence on it for success in the case of PD are important factors.

Incident patients who are eligible for KT represent a paradigm of the benefits of a well-planned strategy of RRT. Their life expectancy is long and the waiting time for transplantation is variable, and usually unpredictable. After KT, long term graft failure

will occur in a significant proportion of cases, meaning reinitiation of dialysis, often indefinitely. The benefits of the PD-first approach will be maximal in this long-term scenery. Importantly, PD will prevent or delay the need for a vascular access, avoiding drawbacks which could persist after KT. Thus, CVC associate an important risk of infection while in place and may injure central veins irreversibly, internal vascular grafts are both a potential source of infection and inflammation, and functioning internal fistulas may carry cardiovascular consequences, including left ventricular hypertrophy. On the other hand, the risk of peritonitis is specific of PD, but there is no evidence that the overall incidence of severe infection after KT is higher in PD than in HD patients. Finally, registry data suggest that PD patients do at least as well, and probably better after KT than HD patients, presenting lower delayed graft function [23] and better patient and graft survival rates [24,25]. Only primary graft thrombosis appears more frequent in PD than in HD patients. As refers to the latter findings, some of them may be the consequence of selection biases, rather than of specific effects of the modality of dialysis.

Older age associates frequently unfavorable conditions for home PD, including inability for self-care, lack of family support and associated comorbidities which may hamper the success of this technique [3–5,16,19]. The combination of older age with diabetes or cardiovascular comorbidity has been claimed to boost an increased risk of mortality on PD, when compared with HD [26]. Even if these limitations are considered, PD may still be underutilized in the elderly. Many of these patients could benefit from this technique, which provides home-based, gentle dialysis to individuals who often display a poor tolerance to HD and in whom maintaining a well-functioning internal vascular access may be a challenge. PD is a good alternative to permanent CVC for HD, particularly in older patients with longer life expectancy [27]. Home or center-based assisted PD facilities have proved efficient to provide PD to older patients who prefer home dialysis but are unable to do self-care [28].

Some registry data have put under question the convenience of PD in subjects with diabetes or cardiovascular disease [6,26]. The unpredictability of the capacity of ultrafiltration and of the pace of decline of RRF cast doubt on the consistency of PD to guarantee an adequate volume control, which may be critical in these patients. Moreover, the use of glucose as an osmotic agent and the peritoneal protein leak may contribute to an aggravation of metabolic disturbances. These drawbacks downplay the old claimed

advantage over HD of continuous, gentle volume control in these cases. However, current PD practice offers instruments to approach these inconveniences, including automated techniques, icodextrin and, in general, glucose-sparing strategies. There is still a concern that some subsets of patients, including those with an antecedent of congestive heart failure, may do not as well in PD as in HD [29]. Interestingly, PD is viewed as a resource for management of patients with severe heart failure and nonterminal CKD [30]. Overall, diabetes and cardiovascular disease should not be considered unfavorable settings for PD, but neither the former view of this technique as a preferable option when these conditions are present is sustained by current data.

Planning RRT in the Patient Who Starts Unplanned

Unplanned start of RRT is an undesirable setting, leading to prolonged hospital admissions, high incidence of early infectious and noninfectious complications and increased mortality rates [15]. Many patients initiating dialysis by this route present unfavorable social and medical characteristics, and a majority have not undergone adequate predialysis care. Most will finally be managed with in-center HD, using CVC for variable, usually prolonged, often indefinite periods of time [31].

The feasibility of PD in patients who start unplanned RRT has been advocated by several studies [32,33]. At first sight, PD is not attractive in this setting, for several reasons. First, urgent catheter insertion and initiation of PD demand specific resources. Moreover, PD is not efficient for emergency dialysis (hyperkalemia, volume overload, pericarditis, etc.). Thirdly, acute-start PD may associate a high incidence of technical complications, including catheter malfunction and dialysate leaks. Finally, the majority of patients in this situation will prefer in-center HD. However, these arguments should not deter from considering PD for an unplanned start. First, this approach will permit patients to view PD as a realistic alternative. In addition, PD will prevent some risks brought by emergency HD, particularly early infections. Unplanned PD does not carry a significant risk of peritonitis [32,33], while the incidence of septicemia is mark-edly lower than in unplanned HD [8]. Even if the patient finally prefers HD, PD may perform as a bridge until maturation of a permanent vascular access. Overall, the PD option should be considered during unplanned initiation of RRT. This approach may be particularly convenient in areas where CVC-related infections represent a major problem.

Anticipating Failure with Planned Technique Transfer

Integral management of ESKD implies that the convenience of any modality of RRT may expire should the personal or medical circumstances of the patient change. The traditional approach was to undertake modality changes only after overt failure of the original technique. The current perception is that a proactive change, before clinical complications appear, may be more beneficial [21]. In practice, the pathway from PD to HD is relatively well established, and planned transfer of patients with impending PD failure (border- line adequacy, ongoing membrane dysfunction) is being increasingly advocated. On the contrary, programmed transfers from HD to PD are less frequent. This may be partly a consequence of the superior technique survival of HD, but many patients who, for different reasons, do not do well on HD are not offered the possibility of changing to PD. Potential indications include exhaustion of vascular accesses, recurrent complications associated to CVC, poor hemodynamic tolerance to HD, recurrent bleeding and changes in the personal conditions of the patient which may benefit from home-based therapies (home HD should be particularly considered in the latter case). PD will do worse as a second-line therapy than as a primary option, but may preferable to continuation of HD under adverse conditions.

Patients who start dialysis after failure of a KT represent a high-risk subgroup, due to frequently delayed reinitiation of dialysis, accumulated immunosuppression, sequelae of complications during primary dialysis and KT and rapid decline of RRF. The latter circumstance could argue against the use of PD in this setting, but the limited information available does not indicate that the modality of RRT has an influence on the outcome of these patients [34]. Remarkably, the incidence of severe infections may be higher in patients re-started on HD, particularly if CVC are used as vascular access [35].

Conclusions

Predialysis care, informed decision by the patient and timely initiation of dialysis are keystones to a successful selection of the modality of RRT

More than 70% of the patients with ESKD are suitable for PD, as compared with (approx.) 95% in the case of HD. Many medical and social factors have been invoked to discourage

the selection of PD as a modality of RRT, but this technique can be used successfully in the majority of these settings.

The PD-first approach has a solid theoretic background, and the suitable patient must be made aware of its potential advantages. Patients with a prolonged life expectancy, and particularly those eligible for KT, may benefit most from this strategy.

Older age associates frequently adverse social and medical conditions for home dialysis. Home or center-based assisted PD facilities have a potential to improve the utilization of PD, in this setting.

There is no conclusive evidence that the presence of diabetes or cardiovascular disease settle a specific preference either for PD or HD.

The majority of patients undergoing unplanned start of dialysis are treated with in- center HD, due both to their characteristics and to care protocols oriented to this modality. Use of PD for an unplanned start may help reduce the incidence of CVC-associated infections, and permit a higher utilization of this technique.

Timely changes of the technique of dialysis should be submitted to the consideration of patients, whenever a complicated course under the current modality is predicted. Inadequacy, ongoing membrane dysfunction (PD to HD), recurrent infections or dysfunction of the vascular access and poor hemodynamic tolerance to HD (HD to PD) are potential settings for this approach.

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