Should Peritoneal Dialysis Be the Preferred Therapy Pre–Kidney Transplantation?

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The impact of pre-transplant dialysis modality on kidney transplant outcomes has been the impetus for many discrepant reports. Although candidacy for kidney transplantation may not necessarily be the main factor in deciding the choice of pre-transplant dialysis modality, certain complications are thought to be associated with one dialysis modality compared with the other and should be acknowledged.

Most of the evidence to date, especially that for lower rates of delayed graft function, indicates an advantage for peritoneal dialysis (PD) over hemodialysis. More importantly, some groups of recipients clearly benefit more from receiving PD pre-transplant, a finding that was recently reported for high-risk adult recipients of expanded-criteria donor organs and pediatric recipients of living-donor organs. On the other hand, PD may be associated with a higher risk of early graft thrombosis. Moreover, the published literature highlights the need for caution in older candidates with a family history of diabetes mellitus because of potential higher risk for new-onset post-transplantation diabetes mellitus in PD patients. Interestingly, prospective studies validating those findings are scarce; most of the published reports have been limited by either small patient numbers or a lack of consideration of other confounding risk factors.

In the present review, we examined the available literature related to the influence of pre-transplant dialysis modality on post-transplant allograft and recipient outcomes.

Key words
Delayed graft function, kidney allograft thrombosis, kidney transplantation outcomes

Introduction
Kidney transplantation remains the treatment of choice for patients with end-stage renal disease (ESRD) (1). Although preemptive transplantation is the preferred therapy (2), most potential recipients require dialysis before transplantation, either because of late referral to nephrology, late diagnosis of kidney failure, lack of a suitable living kidney donor and long wait times for a deceased donor, or ongoing health problems that must be corrected before transplantation.

In these circumstances, clinicians and patients are faced with a decision about the appropriate dialysis modality based on the patient’s functional status, comorbidities, and available home support, and on the nephrologist’s level of comfort in caring for patients on peritoneal dialysis (PD). In the United States, nearly all patients are initiated on hemodialysis (HD); fewer than 10% are started on PD. The reasons are multifactorial, but might at least in part be related to the perception of nephrologists that patient survival is inferior on PD compared with HD (3). The potential influence of dialysis modality on post-transplant outcomes is not usually taken into account when the decision on the dialysis modality is taken.

Here, we review the available literature about the advantages and disadvantages of PD with respect to post-transplant allograft and patient outcomes.

Discussion
Dialysis modality and likelihood of receiving a kidney graft
To assess the relationship between dialysis modality and post-transplant outcomes, the likelihood of receiving a kidney allograft based on pre-transplant choice of PD or HD should be first analyzed.

Snyder and colleagues looked at donor and recipients profiles stored in the U.S. Renal Data System and found that—after adjusting for patient
demographics, years of ESRD, body size, body mass index (BMI), baseline glomerular filtration rate (GFR) at the time of dialysis initiation, ability to work, and other comorbidities such as cardiovascular disease, peripheral vascular disease, and hypertension—patients on PD were approximately 40% more likely to undergo kidney transplantation (4). The authors found no significant differences between the PD and HD patients in the likelihood of being listed for kidney transplantation or receiving a deceased donor compared with a living donor kidney.

The reasons behind the higher proportion of PD patients undergoing kidney transplantation cannot be dissected out from the foregoing analysis. The authors speculated that it perhaps results from a physician perception of PD causing less morbidity and mortality, at least initially, with potentially suitable transplantation candidates possibly being offered PD more frequently. On the other hand, compared with PD, HD might be perceived to offer lower long-term mortality and therefore be chosen for patients who are predicted to remain on dialysis longer. However, the equal proportions of patients on HD and PD being listed for kidney transplantation do not support the latter theory.

Other unmeasured differences in patient characteristics, social and psychological factors, or comorbidities between HD and PD wait-listed patients might play a role. Notably, a more recently published analysis from the U.K. Renal Registry database showed that patients on home HD and PD are more likely to be listed for kidney transplantation than patients on intermittent HD, indicating a healthier patient cohort on home dialysis modalities (5).

**Obesity, dialysis modality, and post-transplantation outcomes**

The epidemic of obesity in the United States has been rapidly spreading, and the high prevalence of obesity in patients starting dialysis reflects the trends in the general population. In 2006, about 34.6% of all patients starting dialysis had a BMI exceeding 30 kg/m² and 17.3% had a BMI exceeding 35 kg/m²; by contrast, in 1995, 19.1% and 9.7% of patients had BMIs exceeding 30 kg/m² and 35 kg/m² respectively (6). Many transplant centers have established a BMI of less than 30 kg/m² or 35 kg/m² as a criterion of eligibility for kidney transplantation in the belief that obesity negatively affects wound healing, creates difficulty in exposing the surgical site, and is associated with lower patient and graft survival. Obese recipients also have longer operating time, higher risk for wound infection, and perinephric hematomas and lymphoceles (6).

Much emphasis is placed on healthy weight during the pre-transplant evaluation, and potential candidates whose BMI exceeds the target are advised to lose weight before surgery. Weight loss is usually difficult to achieve in patients on dialysis compared with the general population, given the restricted diet, the significant amount of time spent on dialysis, and the fatigue related to chronic illness and anemia. Patients on PD are especially disadvantaged, because they may absorb as much as 1000 kcal daily from the dextrose in dialysate. Pellicano et al. (7) used dual-energy X-ray absorptiometry to evaluate longitudinal body composition changes in incident patients on PD and HD. The authors found that PD patients had the greatest increase in total body fat, with a significant increase in visceral fat. Moreover, a significant number of patients continue to gain weight post transplantation, with as many as 72% of patients possibly being overweight at 12 months post transplantation.

Immunosuppressive medications—in particular, steroids—have traditionally been blamed for the post-transplant weight gain, but other factors such as sex, ethnicity, socio-economic status, and improvement of appetite with restoration of kidney function may also play a role. It might be expected that, compared with HD patients, patients on PD would experience less weight gain post transplantation because the significant calorie load from glucose-containing solution has been removed, but that comparison did not reach statistical significance (6).

The problem of weight gain related to dialysis modality should be therefore taken into consideration, and patients should be counseled about the transplant center’s BMI restrictions and the mortality and morbidity risks related to high BMI. Obese patients who have potential living donors and who are expected to undergo kidney transplantation within a year after dialysis initiation may not benefit from pre-transplant PD.

**PD and new-onset post-transplant diabetes mellitus**

New-onset post-transplant diabetes mellitus (PTDM) is a well-recognized complication in kidney graft recipients, and it contributes to increased cardiovascular
risk, mortality, and renal allograft dysfunction. A number of risk factors for PTDM have been identified, including black and Hispanic ethnicities, obesity, and the type of initial immunosuppressive therapy after transplantation—mainly the use of tacrolimus (8).

The potential impact of pre-transplant dialysis modality on subsequent development of PTDM has been the impetus for much debate. Madziarska et al. (9) analyzed 377 kidney graft recipients and found in a multivariate analysis that treatment with PD before transplantation was a risk factor for subsequent development of PTDM \((p = 0.007)\). On the other hand, in a multicenter retrospective study of 2010 consecutive kidney graft recipients, Courivaud and colleagues (10) showed that the pre-transplant dialysis modality has no impact on the subsequent development of PTDM. The results of those retrospective studies should be interpreted with caution, because varying definitions for the diagnosis of PTDM have been used through the years, and screening for diabetes mellitus varies greatly from one transplant center to another, bringing inherent limitations to those observational studies. Older recipients with family history of diabetes mellitus should be cautioned about the potential higher risk of PTDM with PD, but more studies are needed.

Risks of kidney allograft thrombosis

Large-database and single-center analyses have both shown that PD is associated with an increased risk of allograft thrombosis in adults and children alike (11–14). In adults, the overall incidence of allograft thrombosis is less than 1%, but it is higher in pediatric recipients and was found to be one of the most common causes of allograft failure (12). That finding is of particular concern, because as many as 65% of children with ESRD are treated with PD (12). Other than dialysis modality, the stepwise proportional hazards model found a cold ischemia time greater than 24 hours, prior transplantation, and donor age less than 6 years to be significant contributors to thrombosis. The reasons for the association of PD with increased risk for kidney graft thrombosis are unclear. Some hypotheses include the hypercoagulable state associated with PD because of albumin loss in effluent and the increased production of certain coagulation factors. Other plausible risk factors that are difficult to adjust for include surgical techniques and perioperative factors such as hypotension. The use of anticoagulation prophylaxis such as aspirin or heparin may minimize the risk of graft thrombosis in patients on PD, but further prospective studies are needed to validate that hypothesis.

Delayed kidney graft function

Delayed graft function (DGF), a manifestation of acute kidney injury post kidney transplantation, is most often defined as a need for dialysis in the first week after transplantation. The causes are complex and involve donor factors (ischemic injury and inflammatory signaling) and recipient factors (reperfusion injury, innate immune response, and adaptive immune response). The incidence of DGF has been increasing over time and has reached 20% in recent reports. The increase is most likely a result of the increasing use of expanded-criteria donors and non-heart-beating donors (that is, donation after cardiac death) (15).

Mainly because of its association with acute rejection and chronic allograft nephropathy, DGF has been shown to increase the risk of post-transplant complications (15). A recent meta-analysis showed that, compared with patients having good post-transplant kidney function, those with DGF had a 41% increased risk of graft loss (16). Minimizing the risks for DGF is therefore an important aspect of perioperative management. Many studies have showed that pre-transplant PD is associated with a decreased incidence of DGF (4,17–21). One of the possible explanations is that patients on PD have better preserved residual kidney function, and thus require dialysis less frequently post transplantation. The other potential explanation could be “better biocompatibility” of the peritoneal membrane, because the use of more-biocompatible membranes in HD has previously been shown to reduce the incidence of DGF (22). Further exploration of the protective effects of PD on DGF is intriguing; more studies are needed.

Kidney allograft and recipient outcomes

The influence of pre-transplant modality on long-term outcomes of kidney allografts and recipients has been the subject of extensive analyses.

Snyder and colleagues examined the effects of pre-transplant dialysis modality on recipient and graft outcomes in a large cohort of patients (4). Despite the higher transplantation rate in PD than in HD patients, PD patients had higher rates of early graft failure. Interestingly, the potential benefit of low DGF rates
in PD patients appears to be offset by other factors associated with early graft loss. In the study, the adjusted risk for death-censored graft loss was 1.15 times higher in PD than in HD ($p < 0.05$), but mortality and overall graft failure rates were not different.

In contrast, Goldfarb–Rumyantzev and colleagues (23) showed that, compared with PD, HD as the main renal replacement modality immediately before transplantation or as a predominant modality during the ESRD course is associated with increased risk for graft failure and recipient death. In a more recent study, Schwenger et al. (24) analyzed data from 60,008 recipients in the Collaborative Transplant Study. They found that, compared with recipients treated with HD, those who were treated with PD before transplantation had a 10% lower all-cause mortality ($p = 0.01$), but similar death-censored graft survival ($p = 0.39$). The explanation for the superior all-cause survival of PD patients was attributed mainly to a lower rate of cardiovascular death in a subcohort of high-risk recipients and the higher risk of death in HD patients, mainly from cardiovascular causes. Similarly, pediatric recipients, especially of kidneys from living donors, benefited most from PD compared with HD before transplantation. The longer duration of pre-transplant HD adversely affected pediatric renal allograft survival in a linear manner, but the same effect was not observed with pre-transplant PD (17).

Summary
Analyses of the impact of pre-transplant dialysis modality on subsequent kidney graft outcomes has led to much discrepancy in the literature. The retrospective (rather than prospective) nature of the published literature warrants cautious interpretation. Based on recent analyses, the use of PD before transplantation is most beneficial in high-risk recipients with expanded-criteria donors. Pediatric recipients receiving living-donor kidneys have better graft survival if they have been receiving PD before transplantation. The incidence of DGF has repeatedly been shown to be lower in patients on pre-transplant PD, but that finding might, at least in part, be related to better-preserved residual kidney function.

Caution should be used in patients receiving PD who are at high risk for venous thrombosis, because there is evidence of higher risk of early graft thrombosis in those patients. Significant weight gain on PD may influence listing for transplantation and post-transplant outcomes, and therefore PD should not be encouraged in overweight candidates. Moreover, older recipients with a family history of diabetes mellitus should be cautioned of the potentially higher risk of PTDM with PD.

Although more research is needed to depict the true impact of pre-transplant dialysis modality on patient and allograft survival, PD is not inferior pre-transplant, but might in fact be the preferable option in certain groups of recipients.

Disclosures
The authors have no financial conflicts of interest to declare.

References


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