

# Combining Peritoneal and Hemodialysis in the Same Patient: Furthering Precision Medicine in Dialysis Transitions



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Despite decades of experience with both peritoneal dialysis (PD) and hemodialysis (HD), nephrologists around the world continue to debate the optimal dialysis modality. Wide geographic variations exist, with Hong Kong, the pioneer of PD first, having the highest prevalence of PD patients at approximately 70%. In contrast, the United States is currently at 10% to 12%, and Japan stands at approximately 5% PD prevalence.<sup>1</sup> Lately, the U.S. president's executive order has mandated increasing the use of home dialysis modalities over the next 5 years, including the use of PD, necessitating U.S.-based nephrologists to be more cognizant of PD, its outcomes, and its complications.

Recent research has shown that dialysis staff with less training and enthusiasm for PD are associated with lower rates of PD initiation,

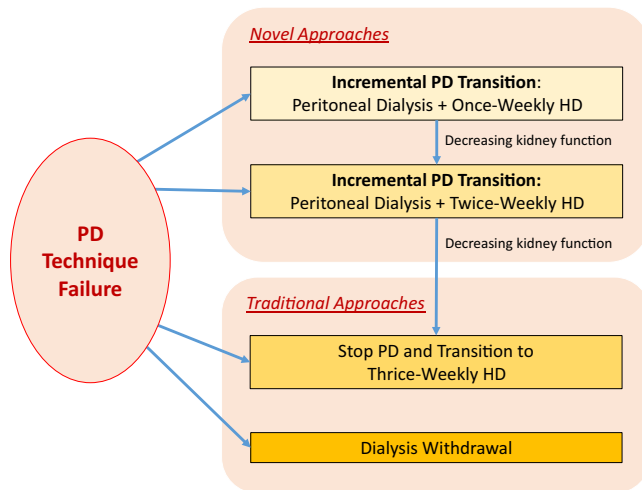
reflecting possibly a negative bias regarding its suitability for patients.<sup>2</sup> Regardless, the incidence rates of PD have risen over the past several years, at least in the United States, possibly reflecting patient preferences for home-based modalities or our increasing awareness and comfort regarding this modality. In addition, the U.S. government has increased reimbursement rates for PD since 2011, which also may have helped hasten the rise of PD. Whether by government mandate, patient preference, physician competence, or changing reimbursement models, the number of PD patients is expected to continue to rise over time. Keeping in mind our own limitations and biases, striving for a more complete understanding of PD will undoubtedly improve outcomes, decrease our own partiality against this modality, and align our treatments to patient preferences.

The fundamental question of whether the PD modality inherently has better outcomes than HD when controlling for patient factors has not yet been answered by randomized trials, despite several attempts to do so and a recent

study suggesting that there are no differences in mortality outcomes.<sup>3,4</sup> In both attempted randomized controlled trials in the United States and the Netherlands, investigators failed to randomize appropriately due to patient preferences for modality type, highlighting that patient preferences remain the driver for selecting the dialysis modality. It is also known that incident PD patients are generally healthier and have higher residual kidney function at baseline compared with HD patients, possibly leading to improved mortality and morbidity outcomes in observational studies. Attempts to overcome randomization issues, including the use of sophisticated statistical modeling techniques as propensity score or instrumental variable analyses have been pursued with some degree of success, but the inherent issue of nonrandomization with residual confounding still persists as a methodological flaw of the observational study design.<sup>4</sup>

Notwithstanding the limitations of observational studies, the quest to improve our understanding of PD outcomes should continue, especially in understanding the complications of this modality and the reasons for its technique failure. In the United States, PD technique failure rates are approximately 20%, 40%, and 55% at 1, 2, and 3 years, respectively.<sup>5</sup> Although PD failure occurs for a variety of reasons, because of peritonitis, inadequate dialysis, catheter malfunction, or psychosocial factors, traditionally many patients had no choice but to convert to thrice-weekly in-center hemodialysis. This is in sharp contrast to the fast-emerging concept of *incremental dialysis*, whereby incident dialysis patients with adequate residual kidney

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**Figure 1.** Traditional and novel options to transition from peritoneal dialysis (PD) to hemodialysis (HD).

function (i.e., native urea clearance  $>3$  ml/min) who meet certain criteria are nowadays expected to transition to twice-weekly HD for the first several months.<sup>6</sup> Over the past several years, the concept of incremental dialysis has gained substantial acceptance in the United States and abroad, given its nature of patient-centeredness and its alliance with the basic principles of *precision medicine*.<sup>7</sup> The University of California Irvine incremental dialysis model that is also practiced at the Veterans Affairs Medical Center in Long Beach, California, has emerged as the prevailing model of twice-weekly HD transition throughout the nation and beyond.<sup>8</sup> Based on our unpublished data, no patients have died out of more than 100 incident dialysis patients who initiated twice-weekly HD since 2014 and maintained this infrequent HD regimen between 3 months to 3 years before they transitioned to thrice-weekly HD. This is in contrast to the high mortality rate during the first year after dialysis transition that has been described relatively consistently on outright initiation of conventional thrice-weekly HD.<sup>6</sup> Nevertheless, the use of incremental dialysis is not quite clear.

More unclear is the utility of other precision medicine-based approaches in dialysis therapy realms, including combining HD and PD. In a recent concept model, Gedney (who is a dialysis patient) and Kalantar-Zadeh<sup>9</sup> proposed translating the incremental model to incident PD patients using shorter dwell times, less daily solution volume, or fewer than 7 dialysis treatment days per week. A gradual transition to more frequent or more intense dialysis therapy over several months can then be used to counter worsening fluid retention and uremia.<sup>9</sup> These authors also suggest that if less frequent PD is desired, PD may be combined with sporadic HD treatments, although there are few data about the benefits and challenges of such combination approaches. To that end, if PD appears to be inadequate on further reduction in residual kidney function, sporadic HD therapies in addition to background PD, such as once-weekly HD, can be considered (Figure 1).

In the current edition of *KI Reports*, Tanaka *et al.*<sup>10</sup> have investigated hospitalization outcomes in patients converted to a combination of PD and HD, a modality that is rarely heard of in the United States or Western Europe. Investigators

matched prevalent HD patients with 42 combined PD and HD patients, most (37, or 88% of the combined PD-HD cohort) of whom were converted from PD due to inadequate dialysis or volume overload. There did not appear to be any significant differences in hospitalization rates between the combination PD-HD cohort versus the HD cohort, but investigators unsurprisingly noted an increase in hospitalizations for dialysis access-related issues in the combined PD-HD cohort, including vascular complications and PD-related infections of 21.7 per 100 patient-years versus 7.2 per 100 patient-years, respectively.

Many readers may take these interesting results to suggest that the combined modality should not be offered and that patients should be switched directly to HD when PD failure occurs given the increased risk of dialysis access complications. However, the fact that total hospitalization rates did not differ between the 2 groups may suggest an alternative approach whereby patients maintain the independence of PD while slowly, instead of abruptly, transitioning to HD (Figure 1). Quality of life, maintenance of independence, and the ability to perform a life-sustaining treatment on one's own schedule is an important consideration. This is especially true in the era of precision medicine, incremental transitions in dialysis, and more intense focus on patient-reported outcomes. Our experience with transitioning patients from chronic kidney disease 5 to dialysis via the University of California Irvine twice-weekly incremental dialysis model for patients who meet eligibility criteria<sup>6</sup> has improved compliance, maintained residual kidney function, and improved long-term outcomes.<sup>11</sup> The transition from full PD to combined PD-HD can be likened as a similar transition

period between chronic kidney disease and HD, one which can potentially avoid the constant hemodynamic changes seen in HD and its associated poor outcomes.

There are inherent limitations to this small, nonrandomized study from Japan,<sup>10</sup> including the lack of individual dialysis PD prescription details before transition and individual patient characteristics that make it difficult to ascertain if adjusting the PD prescription may have prevented them from switching to the combination modality. The small study in a limited geographical area with a homogeneous patient population will also affect generalizability of these findings to other non-Asian countries, especially because most dialysis centers around the world are not capable (logistically or otherwise) of performing such combination dialysis treatments. Furthermore, mortality outcomes in this study and optimal dialysis adequacy targets for combination modality patients overall remains unknown. Although larger studies that investigate the feasibility and outcomes of the combined PD-HD dialysis modality over the long-term are needed, this small but important study points to an avenue to assist patients with the transition from PD to HD.

Ultimately, modality selection must remain the patient's decision, but having an improved understanding of the modalities and its complications, in addition to considerations when transitioning

patients to and from various modalities, will undoubtedly improve the education of our patients, remove our personal biases against the PD modality, and enhance outcomes both here in the United States and abroad. There are many advantages to using precision medicine tools to institute incremental dialysis and combined HD-PD protocols. These include longer preservation of residual kidney function, avoidance of the abrupt transition from PD to thrice-weekly HD on PD technique failure, improved adherence to patient preference, and allowance for a greater patient-centeredness. Although we are uncertain that a combined HD-PD will ultimately become a favorable treatment choice globally, we remain highly enthusiastic of innovative dialysis and nondialysis options and combinations.

## DISCLOSURE

All the authors declared no competing interests.

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