Timing of Initiation of RRT and Modality Selection

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Abstract
There is no shortage of studies and registry data examining outcomes of patients on dialysis and those with a renal transplant. However, recently, there has been a greater focus on the events leading up to the institution of kidney replacement therapy. Associative data suggest that early and consistent predialysis care leads to better outcomes, including greater take-on to home-based therapy, diminished use of tunneled venous hemodialysis catheters, and improved early and even late survival. What transpires during predialysis visits is also important. Simple dissemination of facts to the unprepared patient is unlikely to be effective in moving the patient and family along in the process of the series of choices that have to be made around therapy. A more flexible and circumspect approach is needed, including recognizing when the patient is or is not ready for change. There seems to be no optimal timing of dialysis start that can be applied to the ESRD population as a whole, although the pendulum seems to be swinging back toward symptom-based rather than eGFR-based starts.


Introduction
The patient was referred to a nephrologist in 2005 when he was found to have a serum creatinine of 4.5 mg/dl (eGFR=14 ml/min). He was 75 years old at the time and recalled being seen by a nephrologist approximately 20 years previously, when he was told that he had an atrophic kidney and high BP. Previous creatinine levels were 2.4 mg/dl in 2000 and 2.8 mg/dl in 2003.

He was referred to our hospital’s predialysis clinic. He attended the clinic and was interested in renal transplant. Given his age and previous coronary artery disease and bypass grafting, it was also explained that he should know about his options for dialysis in case a renal transplant was not possible. After receiving dialysis modality education, he decided to undertake peritoneal dialysis (PD) if his renal deterioration progressed and he could not receive a preemptive renal transplant.

He attended the clinic regularly and remained asymptomatic. The serum creatinine increased very slowly. By November of 2007, his creatinine was 6.4 mg/dl (eGFR=8 ml/min). He remained asymptomatic and was working full time. His donor had not proceeded with workup. The patient was also advised to have a PD catheter inserted but declined and decided instead to take an extended golfing vacation over early 2008.

The Patient and Education Predialysis
In patients with identified CKD, education about their disease and its management has been shown to be associated with a number of benefits. These include elective dialysis starts with access in place, reduction in hospitalizations, higher prevalence of patients choosing a home-based dialysis modality, and in those starting with hemodialysis, a reduced prevalence of catheters (1–4). An interesting 20-year follow-up study even found a significant late survival benefit associated with predialysis education (5).

What Constitutes Effective Predialysis Education?
It is assumed that adequate predialysis education involves supplying the patient with information and facts pertaining to the series of decisions that have to be made (Figure 1), including RRT versus maximum conservative care, dialysis versus renal transplant (live or deceased donor), home dialysis versus center-based hemodialysis, and home PD versus home hemodialysis.

This series of decisions can be overwhelming. Furthermore, it is often envisioned that these discussions are taking place with what I call fantasy patients: English-speaking, educated, and health-literate patients and their families. (The recent United Kingdom National Health Service No Decision about Me without Me [6] policy assumes the same fantasy patients.) The reality is that many of these patients do not speak English and have immigrated from other countries and, importantly, other cultures. For example, patient surveys have suggested that patients want to know their prognosis and predicted survival time with ESRD (7). However, an important criterion for taking the survey is the ability to speak English, which essentially excludes many immigrants who may have different value systems than those who are eligible for and agreed to complete the survey. Furthermore, in our culture, patient autonomy is assumed to be the overarching principle guiding decisions about therapy. However, we encounter many families where the spouse and children insist that the patient not be told about the diagnosis and the prognosis.

Often overlooked is the option of nondialytic care. It is important that this be discussed with the patient and family, particularly when the patient is very elderly
or has a number of serious comorbidities. In these patients, dialysis may not extend survival, or any prolongation of survival is spent doing the dialysis or traveling back and forth from a dialysis unit (8). A dispiriting study from Davison (9) suggested that the majority of patients on dialysis, at least in this survey population, regretted the decision to start dialysis. In my experience, very often, the elderly or very ill patient will consider nondialytic care, but the children of the patient will not accept this decision and will convince the patient to undertake RRT. The input of a social worker or someone with expertise in geriatrics can be helpful in this situation.

Furthermore, it is usually during the education process, as the overwhelmed patient is being inundated with information, that home-based dialysis is brought up as one of the decisions that the patient and family have to make. Many patients, already terrified, will reflexively recoil from this suggestion, and the nephrologist explains the low take-on to home therapies as “My patients don’t want to do home dialysis.”

In the early days of our predialysis clinic, the nurse educators supplied information in the form of a patient toolkit that outlined the options for ESRD. The majority of patients never even looked at the material (available in many languages) or quickly misplaced it. We have evolved our education to include motivational interviewing rather than dry dissemination of information (10). The goal is to increase the patient’s own motivation so that they initiate or accept change rather than having it imposed on them. The states of change are listed in Table 1. (The stages of precontemplation to contemplation to preparation to action will be familiar to anyone who has attempted to quit smoking or go on a diet.) Previously, patients were essentially paralyzed and unwilling to consider their options. Motivational interviewing helps patients recognize their current situation and may be helpful when patients are ambivalent about change. The strategies are more supportive than coercive, and the overall goal is to increase the patient’s own motivation, so that change comes from within rather than being imposed by outside forces (11).

A recent and novel analysis of predialysis care, taken from administrative data, suggested that classifying patients as early versus late referral may be too simplistic to examine the process of care leading up to the start of RRT (12). More predictive of optimal start was the number and consistency of clinic visits, especially in the critical period just before dialysis start, rather than the time of first referral. In other words, although it may be preferable for a patient to start seeing a nephrologist sooner rather than later in the course of declining kidney function, it alone is not sufficient to improve outcomes. (This is also congruent with the findings of Finkelstein et al. [13] that a surprising number of patients under usual nephrology follow-up had little information about their disease or treatment options.) Although

<table>
<thead>
<tr>
<th>Stage</th>
<th>Precontemplation</th>
<th>Contemplation</th>
<th>Action</th>
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<tr>
<td>Patient response</td>
<td>“I don’t want to...” Try to understand what is underlying the ambivalence</td>
<td>“I don’t think I can...” Focus on the pros of making a decision but try to overcome the cons</td>
<td>“Tell me more about...” Reinforce the pros of having made a decision and explore the supports needed to overcome any cons related to modality choice</td>
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<tr>
<td>Education</td>
<td>Negotiate what information the patient is willing to receive</td>
<td>Provide more detailed information about options; main focus to provide information that is relevant to the patient’s perceived barriers</td>
<td>In-depth education about access, training, and transplant options</td>
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Figure 1. | Decisions around planning for ESRD. HD, hemodialysis; HHD, home hemodialysis; PD, peritoneal dialysis.

Table 1. Stages of change by Prochaska et al. (34) applied to CKD (10)
Finkelstein et al. (13) were limited by the administrative nature of the data and could not know what the benefit was of frequent and consistent visits, I would suggest that it takes multiple encounters with the patient to prepare them and guide them through the many decisions that have to be made. It is during the frequent visits that the issue of home dialysis can be revisited.

A review of the disposition of patients attending our predialysis clinic showed that, of the patients who progressed to ESRD, the largest number (79 of 153) was initiated on PD, and 15 patients started on home hemodialysis (14). In other words, about 60% of graduates from the clinic initiated a home dialysis therapy. The principal barriers to home dialysis were being a single man (this has been noted before) and lack of interest in this modality by the patient and/or the family.

**Modality Choice**

In the patient who is pursuing therapy for ESRD and is not a candidate for preemptive transplant, education should have the goal of allowing a decision about the type of dialysis. This should not be framed as hemodialysis versus PD but as home dialysis (home hemodialysis or PD) versus in-center hemodialysis. Surveys from several countries have shown that nephrologists believe that about one third of the ESRD population would be appropriate for PD (15,16). However, the prevalence of PD as RRT varies dramatically from country to country: from essentially 0% to >80% where payers promote a PD-first policy. This variation suggests that there are significant determinants of modality choice other than what is most appropriate for the patient.

There is little agreement about patient-related factors and the use of home dialysis in general and PD in particular. The absolute contraindication for PD would be an unusable peritoneal cavity, such as in those with several previous abdominal surgeries, especially if associated with surgical peritonitis, which is more likely to lead to extensive adhesion formation. This may compromise the peritoneal cavity, and in the case of mild adhesions, these can often be lysed at the time of PD catheter implantation using advanced laparoscopic techniques (17). Active inflammatory bowel disease and recurrent diverticulitis put the patient at risk for peritonitis from enteric organisms, and we discourage PD in these patients. However, we and others have successfully performed PD in patients with previous abdominal surgery, including cholecystectomy, colectomy with or without colostomy, hysterectomy, abdominal aortic aneurysm repair, liver transplant, and cystectomy and ileal conduit.

Aside from issues related to a usable peritoneal cavity, there are few other absolute contraindications to PD. Many of these are social, including the living environment. Patients who live alone in one room may not have good social support and, practically, may not have sufficient space to carry out home-based therapy. This restriction applies to both home PD and home hemodialysis. Cognitive or behavioral problems are also a relative contraindication, but often, these patients do not do well with center-based hemodialysis either. We have looked after a patient with paranoid schizophrenia for several years who performs her PD intermittently and is relatively underdialyzed. However, this patient was unlikely to appear for center-based hemodialysis unless brought in by paramedics or police. On balance, we (including the patient) agreed that PD was the better option for her. Where there are restrictions on the basis of infirmity, either physical or mental, the presence of home help, such as family members, can increase the spectrum of patients eligible for PD (18). Jurisdictions that offer home-assisted PD with a visiting nurse also allow patients to undertake that therapy where otherwise they would not have been able to manage by themselves (19,20).

**No PD for You**

During his vacation, this patient became ill and went to hospital. He requested insertion of the PD catheter but was advised that he should not undertake PD because of the risk of peritonitis. Instead, a PermCath was placed. He received several sessions of hemodialysis, felt better, and returned home. He did not want to change to PD, and vascular access creation was deferred, pending clearance of the patient and his donor for kidney transplant.

**Optimal Timing of the Start of RRT: Was It Left Too Late?**

The timing of elective dialysis initiation continues to be a vexing issue and the subject of much debate (21–24). In the early days of maintenance dialysis, patients were commenced when they were symptomatically uremic. The advantage of this approach was that the patients experienced the misery of uremia and the improvement in their wellbeing with the institution of dialysis, and therefore, they recognized its importance by their own experience. However, by the 1990s, the pendulum has swung toward early start or healthy start, which subscribed to the idea that patients should not be allowed to hit bottom and then rescued with dialysis back to wellbeing. It was recognized that, as patients progressed to uremia, they spontaneously reduced their dietary protein intake (25) and therefore, may have eventually commenced RRT in a malnourished state. In many developed countries, the GFR at the initiation of dialysis steadily rose over time, driven at least, in part, by the concept of healthy start.

Many studies have now brought into question the optimal time for dialysis initiation. In a prospective multicenter study in The Netherlands by the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD) Consortium, kidney function was measured by 24-hour urine collections close to the start of dialysis. Using the then-current Dialysis Outcomes and Quality Initiative guideline of renal Kt/V urea of 2.0 per week as a start time, the NECOSAD cohort of 253 patients was classified as timely versus late starters. There was a small survival benefit for the patients with early starts, with the hazard ratio of 1.66 (95% confidence interval 0.95–2.89) in favor of this group. Interestingly, however, the extended survival for the patients with timely starts was 2.5 months, whereas for late starters, the extra time not yet on dialysis was about 4 months. In other words, one interpretation is that all of the patients would have died at the same time, and lead time bias makes the survival look better for the timely start cohort (26).

A number of other observational studies published since the NECOSAD using registry data found progressively reduced mortality if dialysis was started at a lower eGFR (residual kidney function determined by formula and not
24-hour collections). As reviewed recently (27), the association does not prove that starting dialysis with a higher eGFR causes the increased mortality, although this is one possible explanation. In that case, it could be seen as competing risks between the dialysis process itself in the patients with early starts versus the risks of uremic toxicity over the same period of time in the later-start cohort. However, other explanations include the possibility that patients who are sicker have lower muscle mass and serum creatinine, which will, by formula, make the creatinine clearance a higher number, and they do worse not because of a higher eGFR per se but because of their sicker status. Another source of complexity is whether the GFR at the start of RRT is measured or calculated. There is also the issue of lead time bias as mentioned above, wherein a patient starting a treatment earlier may survive on the treatment longer but die at the same time anyway, and survivor bias, where the patients with late starts have to be healthy enough to get to the lower GFR and start treatment. Furthermore, patients with multiple comorbidities may not tolerate the uremic state and get initiated on dialysis at a higher eGFR, but the worse outcome is related to the comorbidity and has nothing to do with the kidney function at dialysis start (27).

The Initiating Dialysis Early and Late (IDEAL) Study was a randomized, controlled study in Australia and New Zealand in patients with stage 5 CKD (28). The study was designed so that patients were randomly assigned to start dialysis when the eGFR was 10–14 ml/min (early start) or continue to receive care and start dialysis when the eGFR was 5–7 ml/min (late start). There was no significant difference in survival between patients in the late- and early-start groups (hazard ratio, 1.04; \( P = 0.75 \)). Interestingly, >75% of the patients in the late-start group initiated dialysis when the GFR had not yet fallen to 7 ml/min as a result of supervening symptoms. The average realized creatinine clearance at dialysis start was, therefore, less different than planned: 12 ml/min in the early-start cohort and 9.8 ml/min in the late-start cohort.

The publication of the IDEAL Study set off a plethora of opinion pieces, but my overall impression is that there is a now a sense of reassurance that patients do not have to start dialysis on reaching stage 5 CKD if they remain asymptomatic. However, there are three points that merit discussion.

First, the elective commencement of dialysis when the patient could perhaps wait a little longer allows for more flexibility in the prescription. This is the concept of incremental dialysis and eases the patient onto the therapy (29). In center-based therapy, incremental hemodialysis could comprise fewer hours per session, fewer sessions per week, or both. For the patient on PD, incremental therapy is a good way to get the patient used to the process without overwhelming them with a regimen at the outset that would be necessary for someone with no residual kidney function. Such a regimen in continuous ambulatory PD could be, for example, two exchanges a day. In patients electing to carry out automated PD, an incremental regimen could be two or three exchanges overnight (not necessarily 9 hours) with a dry day. The dry day obviates the worry about fluid absorption during the long dwell. There is the possibility that the patient will get too comfortable with the reduced regimen (in my experience, more often with patients on in-center hemodialysis than on PD), and therefore, it is important to emphasize repeatedly that the regimen that they are on is less than normal and that they will probably, at some point, have to increase the dose of dialysis as the residual kidney function declines. Although this is a more pleasant and practical way to ease the patient onto dialysis, there is little data on the influence of incremental starts on outcomes.

Second, with early-start dialysis, if there is a technical problem, such as needle infiltration of a fistula, or a non-functioning PD catheter, there is not the urgency to place a PermCath with its attendant risks and problems; instead, there is the luxury of some time to work out the mechanical issues or allow for healing, while essentially reverting the patient to predialysis status until dialysis can be safely recommenced. This is an enormously practical issue in favor of early start but one that does not receive much discussion.

Third, we and others have found that institution of PD is associated with a slowing of the decline of residual renal function and therefore, may help preserve this important function over time (30).

Subsequent Course

The patient continued on three times per week in-center hemodialysis, and in May of 2008, he developed excruciating low back pain. Computed tomography scan revealed active discitis at L1-L2 with associated epidural and right psoas abscess. A vertebral biopsy and local aspiration were performed, which revealed no growth. Blood cultures drawn through the PermCath were positive for coagulase negative Staphylococcus in five of five bottles.

During the hospitalization, the patient agreed to change to PD. The PermCath was removed, and the PD catheter inserted.

PD training proceeded uneventfully, and transplant work-up put on hold pending cardiology re-evaluation and resolution of the spinal infection. The dialysis was uneventful, but in August of 2008, reactivation of the discitis occurred, and vancomycin was reintroduced given intraperitoneally with monitoring of blood levels.

Because the patient was captive (essentially incapacitated by the back pain and in the hospital), it was an easy decision for him to revert to his original choice of PD. In many others, however, when hemodialysis is commenced emergently or urgently, inertia sets in, and conversion to a home-based therapy can be difficult. First, the patient and family have experienced a potentially life-threatening medical event and may be too worn out to consider dialysis at home. Second, there may be no mechanism in place for the patient who had an urgent or emergent start and is already on center-based hemodialysis to receive modality education. Third, patients may become socialized to in-center hemodialysis, finding comfort in the frequent interaction with nurses, technicians, and other patients on dialysis in the in-center unit, and for that reason, they may be reluctant to leave the unit and perform dialysis at home. We segregate patients on urgent-start hemodialysis in a separate small unit while they receive education about their options for RRT to avoid the socialization effect. We and others have used a nurse navigator who meets with the patient with an urgent start and the family after the patient is stabilized to discuss options, including transitioning
to home-based dialysis or starting the process for renal transplant. Of 228 patients with acute-start hemodialysis, the institution of the nurse educator program led to 49 patients transitioning to PD and 22 patients transitioning to home hemodialysis, a dramatic change from before the start of the program, where essentially all patients with acute starts remained on in-center hemodialysis (31).

The task of trying to transition a patient from hemodialysis to PD could also be obviated when there is in place the infrastructure to support urgent-start PD. Acute hemodialysis is still the preferred therapy in patients with life-threatening hyperkalemia or pulmonary edema, just in case the PD catheter does not function well. However, if the patient presents with nonemergent advanced CKD or after the acute hemodialysis, has relieved any life-threatening complications, a PD catheter can be inserted, and dialysis can be commenced immediately with low volumes and the patient in the supine position to reduce the risk of dialysis leak (32). A patient going directly to PD avoids receiving a tunneled venous catheter, with its inherent risk of bacteremia. Other than benefit to the patient, urgent-start PD may be associated with significant cost-savings to the health care system (33). In addition to ensuring that a patient starts on PD, which constitutes less expensive therapy for the same outcome, urgent-start PD is itself associated with an approximately $3000 savings in the first 90 days of therapy according to a recent economic model (33).

Patient Follow-Up

Despite his age, the patient received cardiology, infectious disease, and neurosurgery clearance and received an emotionally related renal transplant in 2010 with excellent immediate graft function. The PD catheter was removed. He continues to do well, although is troubled by neurogenic claudication as a late complication of the vertebral infection.

Conclusions

This patient’s course shows a number of interesting challenges that nephrologists and nephrology educators face when dealing with patients with declining renal function. Most importantly, it takes frequent and consistent encounters to adequately prepare someone for a major life change (in this case, ESRD). Mentioning home dialysis in passing will not be sufficient to engage patients at this difficult point in their lives. Another problem is that, even in an educated, prepared patient who has made a modality choice, the onset of symptomatic uremia can be capricious, and therefore, the patient may end up with a tunneled hemodialysis catheter in any case. For PD, use of embedded catheters and/or urgent insertion of PD catheters may help to obviate this problem. There is much debate about the best time to start dialysis in the nonurgent setting without sufficient discussion about other real-life factors, such as navigation of access problems and, of course, financial incentives for placing patients on dialysis sooner rather than later. Although tangential to the main points of discussion, the irony that the patient was dissuaded from undertaking PD because of the risk of peritonitis and ended up incapacitated with metastatic abscess from a hemodialysis line infection also points to the inherent prejudices in the nephrology community that continue to inform medical practice.

Disclosures

J.M.B. is a consultant for Amgen, Baxter Healthcare, and Otsuka and has given talks for Amgen, Baxter Healthcare, and DaVita Healthcare Partners.

References


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