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Dialysis Patient-Centeredness and Precision Medicine: Focus on Incremental Home Hemodialysis and Preserving Residual Kidney Function



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Summary: An exponential interest in incremental transition to dialysis recently has emerged in lieu of outright three times/wk hemodialysis initiation as the standard of care. Incremental dialysis is consistent with precision medicine, given individualized dialysis dose adjustment based on patient's dynamic needs, leading to reduced patient suffering from longer or more frequent dialysis treatments and improved health-related quality of life. It includes twice-weekly or less frequent hemodialysis treatments with or without a low-protein diet on nondialysis days, or a shorter (<3 h) hemodialysis treatment three times per week or more frequent treatments, a useful approach for home hemodialysis initiation. Peritoneal dialysis also can be initiated incrementally with a shorter dwell time, less daily solution volume, or therapy for fewer than 7 days per week. Subsequent transition to more frequent or more intense dialysis therapy within several months or longer will counter worsening fluid retention and uremia, for example, whenever residual urea clearance decreases to less than 2 mL/min or if urine volume reaches less than 500 mL/d, especially if loss of nocturia ensues. There are many advantages to using precision medicine tools to institute incremental dialysis protocols including preservation of residual kidney function, adhering to patient preference, and allowing for a greater patient-centeredness. Incremental dialysis may become the treatment of choice in End-stage renal disease Seamless Care Organizations (ESCO). This article also features a home hemodialysis patient's experience as a real-world scenario of how individualization of dialysis therapy based on unique patient characteristics and adjustment and shortening of hemodialysis treatment time and frequency led to improved patient experience, compliance with treatment regimen, and increased urine output, and the role of future ESCOs.

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Since 2014, the topic of transition of care in chronic kidney disease has received focused attention, highlighted by a US Renal Data System special study center that is dedicated to focused examination of this emerging topic.^{1,2} In the United States and many other countries and regions of the world, an outright three times/wk hemodialysis initiation is the norm. Until recently, twice-weekly hemodialysis frequency or shorter dialysis treatment time (eg, <3.5 to 4 hours per hemodialysis session) was considered suboptimal and against the standard of care. However, in recent years, an unprecedented interest in, as well as heated debate about, the reinvigoration of less frequent hemodialysis treatment upon transitioning to maintenance dialysis therapy has emerged.³⁻⁶ This so-called *incremental dialysis* is based on the premise that in many patients who initiate dialysis therapy for the first time, substantial residual kidney function still exists, represented by a native kidney urea clearance of more than 3 mL/min or a daily urine output of 600 mL or more.^{3,7} In these patients, usually the majority of incident dialysis patients, a less frequent (<3 times/wk) hemodialysis, or less than a full dose of peritoneal dialysis, during the first months of dialysis therapy is not only adequate, but it also may lead to longer preservation of the residual kidney function.

Among the contributing factors that have led to the increasing enthusiasm about incremental dialysis is the patient-centeredness of the approach, including recent

and old data about the advantages of longer preservation of the residual kidney function.^{8,9} This can be achieved by a variety of effective means, including and in particular via less frequent dialysis therapy and/or shorter dialysis treatment time.⁸ The emerging incremental dialysis protocols appear to be more patient friendly and may lead to less suffering and better health-related quality of life. Although in the United States incremental dialysis often is coined with twice-weekly hemodialysis initiation in the first months of dialysis therapy, also known as the University of California Irvine incremental dialysis protocol,^{10,11} there are different types of incremental dialysis transition prescriptions including even less than twice-weekly hemodialysis at the start (eg, once weekly or less), combined with a low-protein diet on nondialysis days.¹² Shorter hemodialysis treatment times, such as 2 to 3 hours per hemodialysis session, with three or more frequent treatments per week, also may be a useful approach for home hemodialysis initiation and maintenance (Table 1). This may appear in sharp contradistinction to the current expectations of longer hemodialysis time, 4 hours or more per session, to achieve a certain dialysis adequacy threshold (single pool Kt/V >1.2), which sadly often does not account for the residual kidney function given the perceived pressure by the so-called Quality Incentive Program of the Center of Medicare and Medicaid Services (CMS) to achieve these targets. Peritoneal dialysis also can be initiated incrementally,¹³ including with shorter dwell time or less daily dialysate solution volume, or by undergoing therapy fewer than 7 days a week, such as with every-other-day protocols. Less frequent peritoneal dialysis may be combined with sporadic hemodialysis treatments, although there are little data about the benefits and challenges of such approaches. Therefore, an

individual patient's dialysis prescription can be devised based on important characteristics unique to each patient including residual urine output, lifestyle and environmental factors (ie, dietary habits, access to treatment), as well as patient preference. Hence, incremental dialysis initiation via use of precision medicine concepts including offering individualized dialysis dose adjustment based on a patient's dynamic needs not only can enhance both in-center and home dialysis patient experience, but also lead to improved patient longevity, including for in-home dialysis patients.¹⁴

In all types of incremental dialysis, a patient's residual kidney function needs to be monitored judiciously because transition to more frequent or more intense dialysis therapy often is needed at some point in time, usually, but not always, within a few months or 2 to 3 years at maximum, whenever the residual urea clearance decreases to less than 2 mL/min or if urine volume is less than 600 mL/d, especially if nocturia ceases to exist.³ According to a recent consensus report, in addition to a decrease in residual kidney function, there are 8 to 10 other criteria for maintaining less frequent dialysis versus transitioning to more frequent or more intense dialysis therapy to avoid volume overload or worsening uremia.³

Patient perspectives on incremental dialysis generally are positive given the less severe impact on lifestyle and suffering upon transitioning to dialysis therapy. In addition, more effective preservation of residual kidney function (ie, the ability to make urine for longer time while on dialysis), enhances patient preference for incremental dialysis protocols and its synergy with the recent Precision Medicine initiatives in the United States and other nations. As shown in Table 2, different types of incremental dialysis approaches highlight different aspects of

Table 1. Types of Incremental Dialysis Protocols

Type of Incremental Dialysis Protocol	Assumption	Suitability
HD		
Type A: less frequent HD (<3 times/wk)*	Maintaining at least 3 to 4 hours of HD treatment time per session	May be more suitable for in-center HD patients
Type B: shorter HD treatment time (<3 h)	Maintaining at least 3 times/wk HD frequency	Suitable for both in-center and home HD
Type C: any combination of the earlier-described protocols	N/A	Suitable for both in-center and home HD
PD		
Type D: shorter total PD dwell time or fluid volume/d	Maintaining daily (7 d/wk) PD	Home dialysis
Type E: <7 d/wk of PD therapy*	Maintaining standard dwell time and volume	Home dialysis
Type F: any combination of the earlier-described PD protocols	N/A	Home dialysis
Type G: any combination of PD with sporadic HD sessions	N/A	Combination of home and in-center dialysis

HD, hemodialysis; PD, peritoneal dialysis.

Note that in all protocols, residual kidney function needs to be monitored judiciously (monthly to quarterly).

*A low-protein diet (eg, 0.6 to 0.8 g/kg/d) can be used on nondialysis days.

Table 2. Precision Medicine May Allow for Greater Patient-Centeredness of Incremental Hemodialysis Protocols

Patient-Related Aspects	Less Frequent HD per Week	Shorter HD Treatment Time	Comments
Smoother transition to dialysis initiation	+++	++	Once-weekly HD may be considered
Ability to urinate	+++	+++	Any type of incremental dialysis may prolong residual kidney function
More free-time off dialysis therapy	+++	+	Twice-weekly HD may be a better choice for traveling patients or patients who live far from the HD center
Lower likelihood of cramps, hypotensive episodes, or other treatment-related symptoms	+	+++	Cramps also may be related to ultrafiltration rate in addition to HD treatment time
Less brisk fluctuation in fluid and electrolyte levels	+	+++	Twice-weekly HD may lead to larger fluctuations, although this is dependent on residual urine output
Better health-related quality of life and patient satisfaction	+++	++	Less frequent in-center HD: less patient transportation and family/caregiver burden
Better suitability for home dialysis therapy	++	+++	Home HD patients may prefer shorter HD treatment times
Longer preservations of AVF	+++	+/-	Less frequent AVF cannulation may lead to lower likelihood of infectious events

AVF, arteriovenous fistula; HD, hemodialysis.

Similar inferences and comments may apply to incremental peritoneal dialysis comparing fewer than 7 d/wk of peritoneal dialysis versus less dwell time or peritoneal dialysis dialysate fill volume.

patient-centeredness of transition of care in chronic kidney disease. The following section is written by Nieltje Gedney, a 65-year-old woman with end-stage kidney disease for the past 4 years, who has been a home dialysis patient.

PERSPECTIVES OF A HOME DIALYSIS PATIENT

Until recently, incremental dialysis was barely a blip on the dialysis radar. Lately, however, there have been several studies released, the most recent by Kalantar-Zadeh's group regarding this topic.^{4,15} Kalantar-Zadeh's group concluded that preserving kidney function has many benefits, including better survival.^{7,11,16,17} To achieve this, Kalantar-Zadeh advocated that a patient may not need a full dose of dialysis. Recently, he published up to 11 criteria (Fig. 1) to help evaluate who is a good candidate for implementing and benefitting from incremental dialysis.^{3,7} I concur completely with his criteria, based on my personal experience, and my comments follow in parentheses.

1. Good residual kidney function with urine output greater than 0.5 L/d (or residual kidney function [KRU] >3 mL/min). (Well, I am not a scientist, but I think a liter and a half of pee every 24 hours counts.)
2. Limited fluid retention between two conservative hemodialysis treatments with fluid gain less than 2.5 kg (or <5% of ideal dry weight) without hemodialysis for 3 to 4 days. (After going 4 to 5 days without a treatment, I can barely remove 1.5 kg, 2 kg on the rare occasion.)
3. Limited or readily manageable cardiovascular or pulmonary symptoms without clinically significant

fluid overload. (No cardiovascular and limited pulmonary symptoms; if there is excess fluid, it will find its way to my lungs but this would take a long, long time without treatment [ie, weeks, not days], or a precipitating event such as pneumonia.)

4. Suitable body size relative to residual kidney function (This one is debatable, so I am going to ignore it.)
5. Hyperphosphatemia ($P > 5.5$ mg/dL) is infrequent or readily manageable. (Nope, no problem there.)
6. Good nutritional status laboratory test results are consistent, predictable, and if they got much better it would be hard to justify dialysis. (My current status hovers around end-stage renal disease [ESRD] stage 5.)
7. Lack of profound anemia. (Well, this one is and always will be an issue, but frequent, consistent laboratory test results and proper anemia management, including titration of erythropoietin-stimulating agents and iron supplementation, are critical.)
8. Infrequent hospitalizations and easily manageable comorbid conditions. (Yes, except for the anemia, no comorbidity issues. Anything else that presented at the onset of dialysis, such as a high blood pressure and hyperparathyroidism, were and remain resolved without medication.)
9. Satisfactory health-related quality of life. (Well, I tell people I feel better now than I did for most of the 20 years before I started dialysis, does that count?)
10. Use of the criteria on twice-weekly hemodialysis patients should be re-evaluated once a month. (My nephrologist and I do re-evaluate, which is why I dropped from 4 days per week back to 3 days with his full support.)

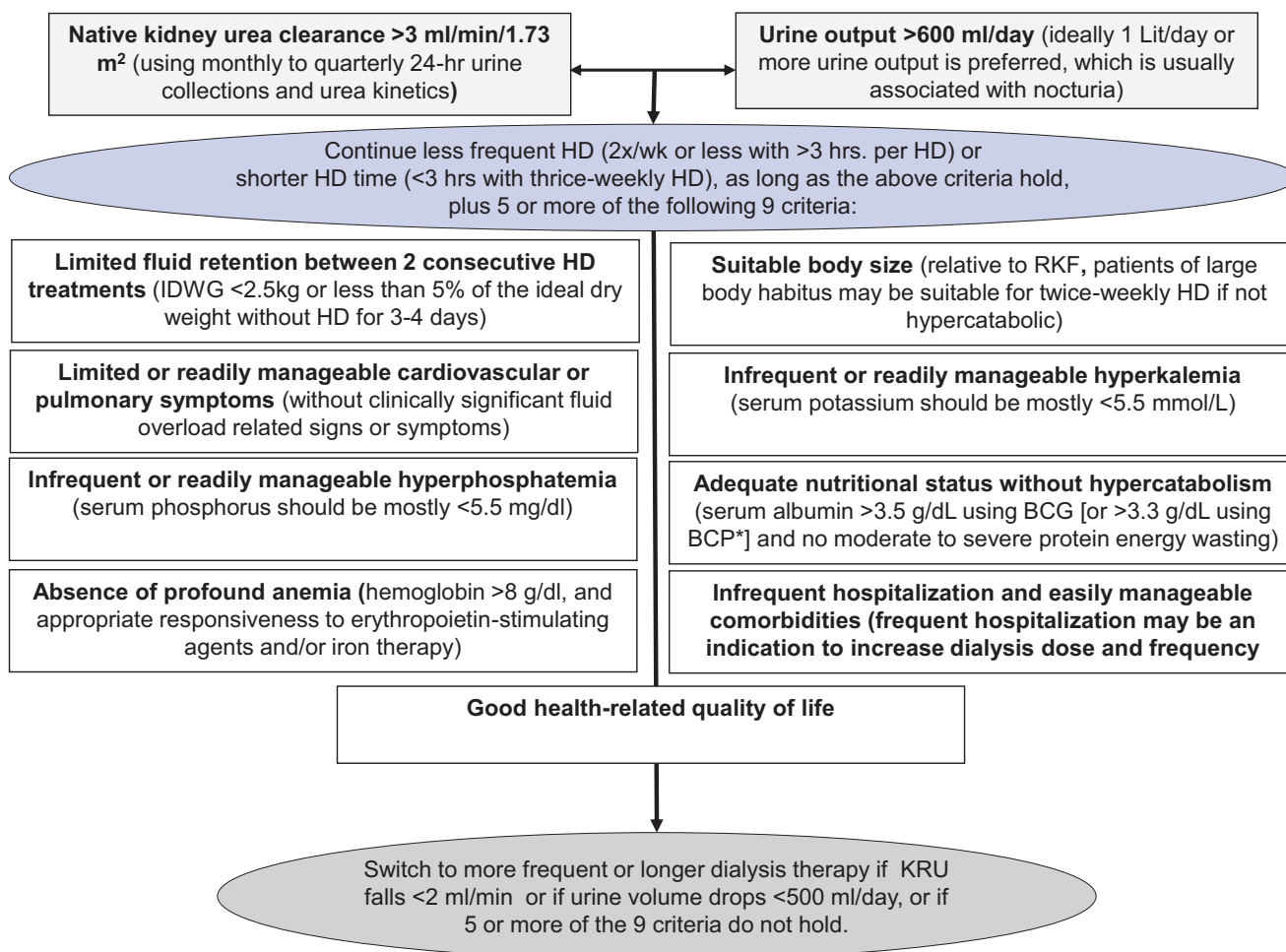


Figure 1. Implementation of the incremental dialysis criteria in practice. BCG, bromocresol green; BCP, bromocresol purple; IDWG, intradialytic weight gain; RKF, residual kidney function. Adapted with permission from Kalantar-Zadeh et al,³ Rhee et al,⁷ and the Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines.¹⁹

Kalantar-Zadeh et al,³ in the 2014 international consensus report on the use of incremental therapy as a conservative approach to treating kidney disease, and several other research reports^{4,9,15} on incremental hemodialysis that have appeared in other major nephrology journals, have spearheaded the effort to introduce incremental dialysis. He also described his University of California Irvine experience with colleagues in a report published in the May 2017 issue of *Seminars in Dialysis*,¹⁰ and spoke in a recent interview with *Nephrology News and Issues*.¹⁸ After reading this, and because I feel so strongly about the benefits of this treatment modality, I was compelled to respond with the patient perspective.

Obviously, I had never heard of incremental dialysis. However, after crashing into dialysis 4 years ago I did know one thing. I had never had any pain with chronic kidney disease for the 20 years before initiating hemodialysis, and I was not about to start living with it now. So, when I came home from those first

days of in-center hemodialysis treatments, 4 hours each, 3 days per week, running hard and fast, feeling washed out from challenging my fluid intake until I cramped, and in serious pain, I questioned opting into this treatment program.

Then one day, a few of us were sitting in the waiting room at the dialysis clinic. As all good dialyzers love to do, we talked among ourselves, sharing war stories. I was describing how awful the pain was as I entered my fourth hour of treatment (think sharp, red hot burning poker imbedded in my kidneys) and a nice young man who had been doing home hemodialysis (until forced to return in-center when his care partner left) said, “You know you can sign yourself out early, right?” Well, I did not have to ask twice.

As soon as the burning pain started in hour four, I said I wanted off. The nurse did what I asked, albeit reluctantly. I continued to do this for the next month. And as I did, a small miracle occurred. I came bouncing into dialysis, feeling great, did my 3 hours, took off my 0.5 kg of

fluid, refusing to challenge fluid removal (a barbaric practice, in my opinion), and left dialysis feeling even better than when I arrived. I also noticed that, in doing this, I found that the need to urinate after treatment greatly increased. It was as if 3 hours unlocked the flood gates, whereas 4 hours slammed the door shut.

Now it may surprise you to learn this, but I like to pee. In fact, I am passionate about it. I want to hang on to it at all costs. When my nurses told me they do not count residual kidney function because they know I will lose it anyway, well, I was devastated. No, I said. Not me.

After the first month of shortened treatments, my laboratory test results were so good that the nephrologist said we could cut back to 2:45 minutes of treatment time. Even better. I knew the nurses had been taking bets that after those first 30 days of signing myself out, I was going to fall on my sword. Miraculously, it did not happen, and we reached a new level of respect for each other.

I maintained this philosophy of no pain is a definite gain as I continued my dialysis journey. So, when I started training for home hemodialysis, the same thing happened. My treatment schedule went to 4 days per week, 3 hours per day, 450 blood flow, and so forth. A week of that and I was crying uncle, or nurse, as the case may be. We slowed things down, decreased my schedule, and I was back to bouncing off the walls with energy.

I asked the doctor why they did not start people off slower and work up their tolerance, and he said, "People will not accept more time, so we just give them the maximum to start." Hence, you now have created a population of patients who have resigned themselves to a life of living to dialyze, no matter how bad they feel. "It is what it is," they are told. Not me. I dialyze to live.

Enter incremental dialysis. One day, I began to encounter studies on incremental dialysis and the importance of residual kidney function. I started reading. It seems there is increasing evidence that simply applying a standard three times/wk hemodialysis dose to all patients with no consideration of residual kidney function is no longer appropriate. The hemodialysis prescription should be tailored to the needs of the individual, and it should be dynamically adjusted as the residual kidney function declines. Such measures may improve patient experience and clinical outcomes in hemodialysis. It made sense.

Well, fast forward 4 years or so, and my dialysis journey has taken me down a road I never dreamed I would walk again. I am back on my advocacy soapbox (my favorite spot since my first job working on Capitol Hill at age 16), devouring everything I could possibly learn about dialysis, state-of-the-art practices, theories, and so forth. I am passionate about optimal dialysis, and avoiding a one-size-fits-all treatment mentality. For me, as

studies continue to support, home hemodialysis and incremental dialysis have been key to achieving the best quality of life possible: physically, mentally, and psychosocially.

I have never wavered from my innate philosophy of no pain is gain, and if something in my treatment causes me to feel off, I work to track down the culprit: a setting is off or something needs changing (time, temperature, frequency). Being on dialysis is like being a detective, and the one thing you learn about dialysis is that it never stays the same. We are constantly tracking down clues. However, I always noticed there seemed to be a set point. A certain amount of dialysis, performed slowly, was like a trigger, opening the floodgates, and allowing me to urinate plentifully and feel great. Push the envelope, and those floodwaters slowed down to a trickle, and I took longer to recover after treatment, and felt worse.

I have learned that, basically, keeping those floodgates open, or peeing, is a very good thing. More and more studies are showing that the longer one keeps residual kidney function the better the benefits, including greater patient longevity and better fluid and phosphorus management, and, most importantly, better quality of life. Seriously? Who would have thought that peeing could be the key to a better life?

Let me be very clear. I am not under any misguided delusions that my kidneys will magically heal themselves, and I will be looking at dialysis from my rearview mirror. I am not living in denial. I am not trying to get off of dialysis. I will be the first to tell you that I look forward to my two to three weekly oil changes. They are like a gas and go. It recharges my fuel cells so I can hit the ground running. Ironically, I will be the first to tell you that I am grateful for starting dialysis. It actually changed my life for the better, and supplied the final missing puzzle pieces to allow me to reach optimum health for my age and with my chronic conditions. I do NOT want to give this up.

Do I believe in longer, slower, more frequent dialysis? Absolutely. Obviously, the degree of residual kidney function, if any, the cause of chronic kidney disease, the longer one is on dialysis, and monthly laboratory test results are all factors in determining an optimal course of dialysis treatment. But everyone is different and starting everyone on 6 days a week of nocturnal makes as much sense as starting everyone on 2 days of 2.5-hour treatments. There is an optimal treatment for every dialyzer. It is up to you and your team to find it, monitor it, and change it as needed, including more or less frequency and time, as symptoms, laboratory test results, and quality of life dictate.

When I started dialysis, I knew nothing. But I had one mantra. I did not do pain. If it made me feel worse, then something was not right. When my questions went unanswered, I was left to figure out what worked through trial

and error. Intuitively, and with a modicum of luck, I stumbled on incremental dialysis, long before I knew of its existence. I am glad I did. For me, it has meant achieving near-perfect health, an amazing quality of life that allows me to travel 3 weeks out of every month or more, and resume a meaningful life of work and advocacy. At 65, living with what is essentially a terminal illness, what more could I ask for?

CONCLUSIONS

Given the recently heightened interest and enthusiasm about incremental transition to dialysis in lieu of outright three times/wk hemodialysis initiation as the traditional standard of care, there is an unprecedented opportunity for implementing precision medicine in initiating dialysis therapy based on the personalized needs of the patient. This individualized dialysis dose adjustment derives from the patient's unique and dynamic constellations and can lead to reduced suffering from longer or more frequent dialysis treatments and improved health-related quality of life. Although incremental dialysis often includes once- or twice-weekly hemodialysis treatment initiation with or without continuation of a low-protein diet on non-dialysis days, a shorter (<3 h) hemodialysis treatment while maintaining three times/wk or more frequent treatment is another useful approach for incremental initiation of home hemodialysis. Incremental peritoneal dialysis includes shorter dwell time, less daily solution volume, or therapy for fewer than 7 days per week. There are many advantages to using precision medicine tools to institute incremental dialysis protocols including preservation of residual kidney function (ie, ability to make urine for a longer time), adhering to patient preference, and allowing for a greater patient-centeredness in the creation of treatment plans.

Given the plans by the CMS to pursue a comprehensive ESRD care model to identify, test, and evaluate new ways to improve care for Medicare beneficiaries with ESRD, including ESRD Seamless Care Organizations or other integrated care models, CMS and other stakeholders may partner with practicing nephrologists and investigators to examine the utility of incremental dialysis in these innovative models of the future. These models are expected to be patient-centered and strive to build on Accountable Care Organization experience. Hence, incremental dialysis may become an important cornerstone of the ESRD Seamless Care Organizations and other Accountable Care Organizations or integrated models.

It is important to note that incremental dialysis protocols stipulate frequent and close monitoring of a patient's clinical condition, in particular changes in residual

kidney function (urine volume and urea clearance), volume status, and disarrays in electrolytes and minerals, among others, so that timely transition to more frequent or more intense dialysis therapy can be implemented to avoid worsening fluid retention and uremia (eg, if residual urea clearance decreases to <2 mL/min or if urine volume decreases to <0.5 L/d), which usually is heralded by loss of nocturia. The patient's direct experience should be the focus of future studies on incremental dialysis to ascertain how individualization of dialysis therapy based on unique patient characteristics and adjustment and shortening of hemodialysis treatment time and frequency can lead to improved patient experience, compliance with the treatment regimen, and maintaining residual kidney function with good urine output, as well as superior outcomes including the patient's longevity. To that end, incremental home hemodialysis therapy is an important target in implementing precision medicine in a real-world scenario of end-stage kidney disease management.

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